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**Alice DEMESMAEKER**

# LA MORBI-MORTALITE PAR SUICIDE : DE L'EPIDEMIOLOGIE LONGITUDINALE A L'EVALUATION D'UN DISPOSITIF DE PREVENTION

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**Jury**

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|---|---|---|
| Pr Catherine MASSOUBRE | Université de Saint-Etienne | Rapporteur |
| Pr Émilie OLIE | Université de Montpellier | Rapporteur |
| Pr Guillaume VAIVA | Université de Lille | Invité |
| Pr Ali AMAD | Université de Lille | Directeur |
| Pr Emmanuel CHAZARD | Université de Lille | Directeur |

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# RESUME

Les patients présentant un trouble psychiatrique ont une diminution de leur espérance de vie en lien avec un taux élevé de suicide et aux comorbidités non psychiatriques. De plus, les patients ayant fait une tentative de suicide (TS) sont particulièrement à risque de récidive et de décès prématuré.

Premièrement, nous avons tenté d'identifier des facteurs de risque de récidive avec des approches statistiques innovantes. Ainsi, nous avons pu montrer que patients ayant un trouble de l'usage d'alcool et ayant consommé de l'alcool lors de leur TS, les patients souffrant d'un trouble anxieux, ceux ayant fait plus de 2 TS et enfin ceux qui consomment des benzodiazépines et/ou des hypnotiques ont un risque élevé de récidive.

Ensuite, nous avons estimé le taux de décès par suicide après une TS à l'aide d'une méta-analyse. Nos résultats ont montré un taux de 2,8% à 1 an. Puis, nous avons recherché les causes de décès dans la cohorte Vigilans. Un an après la TS, les causes les plus fréquentes de décès étaient le suicide et les causes cardiovasculaires.

Enfin, nous avons montré un exemple d'évaluation d'un dispositif de prévention du suicide. Nous avons évalué l'efficacité de la formation d'agents sentinelles dans les maisons de retraite. Nos résultats montrent une amélioration des connaissances sur la crise suicidaire et une diminution du nombre de TS après la formation.

En conclusion, la diminution de la morbi-mortalité des suicidants passe par une prise en charge globale : par la prévention du suicide, mais également par la prise en charge des pathologies non psychiatriques.

Mots-clés : suicide, tentatives de suicide, épidémiologie, prévention, mortalité

# SUMMARY

Patients with a psychiatric disorder have a decreased life expectancy associated with a high rate of suicide and non-psychiatric diseases. In addition, patients who have attempted suicide (SA) are at particular risk for re-attempt and premature death.

First, we tried to identify risk factors for re-attempt with novel statistical approaches. Thus, patients with an alcohol use disorder and with an acute alcohol use during their SA, patients with an anxiety disorder, those who had more than 2 SAs and those who consumed benzodiazepines and/or hypnotics had a high risk of re-attempt.

Then, we estimated the rate of death by suicide after SA using a meta-analysis. Our results showed a rate of 2.8% at 1 year. Then, we searched for causes of death in the Vigilans cohort. One year after SA, the most common causes of death were suicide and cardiovascular diseases.

Finally, we showed an example of an assessment of a suicide prevention program. We evaluated the effectiveness of training gatekeepers in nursing homes. Our results showed an improvement in knowledge about the suicidal crisis and a decrease in the number of SAs after the training.

In conclusion, the reduction of the morbidity and mortality of those who have attempted suicide requires a global management: by suicide prevention, but also by the management of non-psychiatric diseases.

Keywords: suicide, suicide attempts, epidemiology, prevention, mortality

# TABLE DES MATIERES

# INTRODUCTION

Depuis plusieurs décennies, la littérature scientifique a mis en évidence une diminution de plus de dix ans de l'espérance de vie chez les personnes souffrant d'un trouble psychiatrique par rapport à la population générale (1–3). En 1937 et 1942, les travaux de Malzberg et Alström mettent déjà en évidence un taux de mortalité six fois plus élevé chez les patients souffrant de mélancolie et deux fois plus élevé chez ceux souffrant d'un trouble bipolaire par rapport à la population générale (4,5). Plus tard, en 1952 et 1966, Stenstedt puis Perris et Elia ont alors estimé que l'espérance de vie moyenne serait réduite de 15 à 26% chez les sujets souffrant d'un trouble bipolaire (5). Aussi, les patients admis en hôpital psychiatrique entre les années 1920 et 1940 avaient une surmortalité due à la tuberculose, les maladies respiratoires et infectieuses (6). Cependant, dans les années 1960, une étude menée à New York retrouvait un risque de décès par suicide 8 fois plus élevé chez les personnes souffrant d'un trouble psychiatrique (7).

A l'heure actuelle, les études font le constat que l'espérance de vie serait considérablement diminuée chez les personnes souffrant d'un trouble sévère tel que la schizophrénie et les troubles de l'humeur ou d'un trouble lié à l'usage d'alcool (8–11). Quel que soit le trouble, les sujets présenteraient un risque plus élevé de décès par suicide mais également un risque plus élevé de décéder d'une maladie non psychiatrique (12). En effet, une méta-analyse estimait que les causes de mortalité les plus fréquentes chez les sujets souffrant d'un trouble psychiatrique seraient les maladies et affections médicales non psychiatriques encore appelées les causes d'origine « naturelle » (67,3% des cas) puis les causes d'origine externe tel que le suicide, les accidents, les homicides (17,5% des cas) (13).

Parmi les causes médicales non psychiatriques, les plus fréquentes seraient les causes cardiovasculaires (27,3%) et les cancers (18,1%) (8). Cependant, on observe une surmortalité par rapport à la population générale pour toutes les maladies et affections médicales (14,15). Les patients souffrant d'un trouble psychotique ont des taux élevés de décès par maladie du système respiratoire et endocriniennes alors que les patients souffrant de troubles dépressifs ont une surmortalité par tumeurs, maladies cardiovasculaires et du système respiratoire. Ceci pourrait s'expliquer par la présence de facteurs de risque fréquemment associés à ces troubles tel qu'un mode de vie plus sédentaire, une plus forte consommation de toxiques comme le tabac, une moins bonne observance des traitements, une moins bonne prise en charge des comorbidités non psychiatriques et les effets secondaires des traitements psychotropes (1,14,16,17).

D'autre part, plus de 10% des sujets souffrant d'un trouble psychiatrique décèdent par suicide (8,18). La surmortalité par suicide serait la plus importante chez les personnes souffrant d'un trouble bipolaire (avec un taux de mortalité par suicide multiplié par 15 par rapport à la

population générale), ceux souffrant d'un trouble de la personnalité borderline, de dépression et d'anorexie mentale (12,14). A contrario, les personnes souffrant d'un trouble de l'usage d'alcool ont les taux les plus élevés de décès pour les autres causes externes tel que les accidents et homicides (15).

La sortie d'hospitalisation en psychiatrie semble également être une période à risque. Ainsi, la mortalité par suicide serait très élevée dans les mois suivant une sortie d'hospitalisation en psychiatrie (19). Les patients hospitalisés pour un épisode dépressif sévère, une schizophrénie ou un trouble bipolaire seraient les plus à risque de décéder par suicide lors de la sortie d'hospitalisation (20). Néanmoins, les maladies cardio-vasculaires sont la principale cause de mortalité à moyen et long terme (21,22).

Enfin, avec environ 16 millions de TS par an dans le monde, le taux de tentatives de suicide (TS) serait vingt fois plus élevé que le nombre de décès par suicide (23). L'espérance de vie après une TS serait diminuée de 8 à 20 ans selon l'âge de la première TS (24). Plus la TS survient précocement au cours de la vie, plus le risque de développer un trouble mental chronique, de décéder par suicide mais aussi de développer une maladie physique au cours de la vie est élevé (25). En outre, les troubles psychiatriques tel que l'épisode dépressif caractérisé, le trouble anxieux et le trouble de stress post-traumatique et le trouble de l'usage d'alcool sont associés à un risque plus élevés de TS (26) et l'antécédent de TS est l'un des principaux facteurs de risque de décès par suicide (27). C'est ainsi que les patients souffrant d'un trouble psychiatrique et ayant un antécédent de TS ont deux fois plus de risque de décéder par suicide (28).

En conclusion, les principales causes de morbidité et de mortalité en psychiatrie semblent être les affections médicales non psychiatriques (ou causes d'origine naturelle), le suicide et les tentatives de suicide.

Avant de nous intéresser à l'analyse de la morbidité et de la mortalité dans les troubles psychiatriques, il est important de définir comment sont classées les causes de morbidité et de mortalité et de définir l'ensemble des termes utilisés. En effet, la séparation des causes de décès en deux catégories distinctes (les causes d'origine naturelle et externes) peut paraître évidente bien que ce ne soit pas le cas, comme les définitions autour du suicide. Certains termes n'ont, par exemple, jamais été clairement définis et d'autres ont leur utilisation qui semble différer selon les pays (29–31).

## 1. Les classifications des causes de décès.

### a. Causes naturelles et non naturelles.

La classification des causes de décès en causes d'origine naturelle ou d'origine externe ou (non naturelle) est issue de la médecine légale et est largement répandue dans la littérature scientifique (29). En effet, depuis le début du XXe siècle, il apparait que les décès sont certifiés et enregistrés selon quatre « modes de décès » : naturel, accidentel, suicide et homicide (32).

Plusieurs définitions d'une cause d'origine naturelle ont ainsi été proposées : « décès lié à un événement corporel interne non influencé par des événements extérieurs », « décès causé par une maladie, totalement indépendant de tout facteur juridiquement significatif » (33). Le terme de mort « non naturelle » est alors défini comme « causé par un événement extérieur » et regroupe les suicides, accidents et homicides (30).

### b. La classification internationale des maladies.

Depuis plusieurs décennies, le codage des maladies s'effectue à l'aide de la Classification Internationale des Maladies (CIM). *La classification des causes de décès* est présentée la première fois en 1893 lors d'un congrès à Chicago par Jacques Bertillon. Depuis 1945, sa publication a été confiée à l'Organisation Mondiale de la Santé (OMS). La CIM est depuis actualisée tous les dix ans. Actuellement, l'Organisation Mondiale de la Santé (OMS) recommande que le codage de la morbi-mortalité s'effectue avec la CIM-11.

Lors d'un décès, un certificat de décès est établi par le médecin qui atteste de la mort. La cause de décès est ensuite codée à l'aide de la CIM avec des codages spécifiques pour les décès de cause externe. Cet outil de codage international permet des comparaisons des taux de décès dans le temps et entre les différents pays (34). Son utilisation a permis d'établir des statistiques descriptives sur la mortalité et ses causes, dont le suicide et d'identifier des groupes à risque. Cependant, les informations contenues dans les certificats de décès sont limitées et nécessitent en général plusieurs années avant d'être exploitables. De plus, établir la cause de décès lors de la constatation de la mort peut s'avérer difficile notamment lorsqu'il y a une ambiguïté sur le mode de décès. Par exemple, en cas d'intoxication médicamenteuse il peut persister un doute sur une origine accidentelle ou suicidaire et donc sur le codage associé. Il peut alors être intéressant de réaliser une autopsie psychologique en effectuant une enquête rétrospective sur l'intention du défunt concernant sa mort. Cette enquête est menée auprès des proches en interrogeant sur les actions, le comportement et le caractère du défunt pour déterminer la cause de décès (32,35).

Nous avons désormais un aperçu de la manière dont les décès sont actuellement classés selon le mode (d'origine naturelle ou externe) et le codage de la CIM. Nous allons ensuite concentrer notre propos sur la mortalité par suicide en proposant quelques données épidémiologiques, les principales définitions du suicide et sa classification dans la CIM-11 avec les enjeux autour des causes inconnues de décès.

## 2. La mortalité par suicide

### a. Épidémiologie

On dénombre environ 700 000 décès par suicide à travers le monde chaque année, dont un peu moins de 9 000 en France (36,37). Néanmoins, les taux de suicide dans le monde ont diminué au cours des dernières décennies (23). Par exemple, le taux de mortalité standardisé en France a diminué de 16,86 pour 100 000 habitants en 2011 à 13,21 pour 100 000 habitants en 2016, selon le registre national des décès français " CépiDc " (37). Dans les pays à revenus élevés, la pendaison et l'utilisation d'armes à feu sont les méthodes de suicide les plus utilisées (38).

Dans les revues de littérature de Fazel et de Chesney, chez les patients souffrant d'un trouble psychiatrique, les principaux facteurs de risque de décès par suicide identifiés sont le sexe masculin, trouble de la personnalité borderline, l'anorexie mentale, la dépression, le trouble bipolaire, le trouble de l'usage de substances ainsi que l'antécédent personnel et familial de TS (12,23). Parmi les personnes décédées par suicide on estime que 90% souffraient d'un trouble psychiatrique et notamment d'un trouble de l'humeur (39). L'amélioration de la prise en charge des troubles psychiatriques paraît donc capitale si l'on souhaite poursuivre la diminution du nombre de décès par suicide.

### b. Définition

Le terme « suicide » issu du latin *sui* (soi-même) et *caedere* (se tuer) aurait été introduit pour la première fois au XVIIe siècle par Sir Thomas Browne (40).

Plusieurs définitions ont été suggérées au cours des années :

- " tout cas de mort qui résulte directement ou indirectement d'un acte positif ou négatif accompli par la victime elle-même et qu'elle savait devoir produire ce résultat" (Durkheim, 1897/1951)

- "Le suicide est un acte conscient d'annihilation auto-induite, mieux compris comme un malaise multidimensionnel chez un individu dans le besoin qui définit un problème pour lequel le suicide est perçu comme la meilleure solution" (Shneidman, 1985)
- " Le suicide est un acte à l'issue fatale que le défunt, sachant ou s'attendant à une issue fatale, a initié et réalisé dans le but de provoquer les changements qu'il souhaitait" (OMS/EURO, 1986)

Finalement, en 2014, en s'appuyant sur les précédentes définitions, l'Organisation Mondiale de la Santé (OMS) a défini le suicide comme " l'acte de se donner délibérément la mort " (41).

### c. Classification du suicide dans la CIM

Dans la CIM, 1903 à 1948, les cas de suicide ont été classés dans les "affections produites par des causes externes". A partir de 1948 (CIM-6) et jusqu'en 1965 (CIM-8), cette section a été renommée "Accidents, empoisonnements et violences" avec une sous-catégorie "suicide et blessures auto-infligées". Enfin, dans la CIM-10, une sous-catégorie "automutilation intentionnelle" a été créée. Le suicide est actuellement classé dans la CIM-11 dans les « causes externes de morbidité et mortalité » et la sous-catégorie « automutilation intentionnelle ».

### d. Les causes inconnues

Plusieurs questions ont été soulevées ces dernières années autour de la fiabilité des données de mortalité qui sont utilisées (42–44). En effet, alors que le taux de décès par suicide apparaît déjà comme étant très important, ce taux établi grâce aux certificats de décès pourrait être sous-estimé (34,45). En France, on estime que la prévalence du suicide obtenue à partir des certificats de décès est sous-estimé de 10% (46,47). Parmi les arguments avancés par les auteurs, le décompte des suicides pourrait être sous-estimé notamment à cause d'une mauvaise classification des suicides en décès de cause inconnue, de cause accidentelle ou d'intention indéterminée (42–44). La diminution du nombre officiel de décès par suicide et la baisse qui était observée depuis plusieurs années pourrait s'expliquer en partie par la sous-estimation du suicide dans les données utilisées.

Au-delà de la mortalité par suicide, les TS sont l'une des principales causes de morbidité dans les troubles psychiatriques. Les définitions autour des comportements suicidaires ont fait l'objet de controverses ces dernières années (31,40). En effet, plusieurs termes sont couramment utilisés comme les lésions infligées non suicidaires (ou automutilations), les

tentatives de suicide, le parasuicide et les passages à l'acte auto-agressifs. Alors qu'ils font tous référence à des automutilations, ils se distinguent par l'intentionnalité suicidaire. Bien que l'intentionnalité d'un geste soit difficile à établir, ces termes ne sont pas interchangeables et l'établissement de définitions claires et précises pour classer l'automutilation avec ou sans intention suicidaire est nécessaire pour améliorer les travaux sur le suicide. Nous allons donc dresser un tableau des principaux termes employés dans la littérature, leurs définitions et quelques données épidémiologiques.

## 3. Autres définitions et données épidémiologiques autour du suicide

### e. Les lésions infligées non suicidaires

Les lésions infligées non suicidaires ou *non suicidal self injury* (NSSI) se définissent par une automutilation intentionnelle mais sans intention suicidaire. Elles regroupent plusieurs comportements comme les scarifications, brûlures, etc. Les lésions infligées non suicidaires ont été définies par le DSM-5 comme (48): « Au cours de l'année écoulée, le sujet a provoqué, pendant au moins 5 jours, des lésions auto-infligées intentionnelles sur la surface de son corps, susceptibles de provoquer saignement, contusion ou douleur (p. ex. coupure, brûlure, coup de couteau, coup, frottement excessif), en supposant que la blessure ne conduise qu'à un dommage physique mineur ou modéré (c.-à-d. qu'il n'y a pas d'intentionnalité suicidaire). L'absence d'intentionnalité suicidaire a été indiquée par le sujet ou peut être déduite par l'accomplissement répété par le sujet d'un comportement dont il sait, ou a appris, qu'il était peu probable qu'il entraîne la mort. […] »

Ces automutilations aurait une finalité intra-personnelle (soulager un affect négatif) et interpersonnelle (augmenter le soutien social ou diminuer les demandes sociales) (49–51). Leur prévalence varierait de 17 à 60% au cours de la vie et seraient plus fréquents à l'adolescence et au début de l'âge adulte (52). Les lésions infligées non suicidaires sont associés à de multiples facteurs comme la contagion sociale, les facteurs de stress interpersonnels, la dysrégulation émotionnelle et les expériences de vie négatives vécues dans l'enfance (52).

### f. Les conduites suicidaires et tentatives de suicide

Les *conduites suicidaires* regroupent les TS et les suicides aboutis (39).
Les définitions de la TS de Beck et O'Carroll sont les plus utilisées dans la littérature :

- "une situation dans laquelle une personne a exécuté un comportement mettant réellement ou apparemment sa vie en danger avec l'intention de la mettre en péril, ou de donner l'apparence d'une telle intention, mais qui n'a pas entraîné la mort" (Beck)(53)
- « Un comportement potentiellement auto-agressif avec une issue non fatale, pour lequel il existe des preuves (explicites ou implicites) que la personne avait l'intention à un certain niveau (non nul) de se tuer. Une tentative de suicide peut ou non entraîner des blessures. » (O'Carroll)(31)

La définition des conduites suicidaires du DSM-5 est basée sur la définition proposée par O'Carroll en 1996. Ainsi, le DSM-5 a ainsi défini *le trouble conduite suicidaire* selon les critères suivants (48) : « Au cours des 24 derniers mois, le sujet a fait une tentative de suicide. Une tentative de suicide est une séquence de comportements initiés par un individu qui, au moment de l'initiation, s'attend à ce que cet ensemble d'actions conduise à sa propre mort. (Le « moment de l'initiation » est l'instant où le comportement se manifeste par l'utilisation d'un moyen). […] »

La prévalence des TS au cours de la vie se situerait entre 1 et 5 % (26,54). Elles peuvent être classées selon la violence de la méthode utilisée. C'est ainsi que les intoxications médicamenteuses volontaires (IMV) sont considérées comme des TS non violentes et les autres méthodes (pendaison, noyade, suffocation, phlébotomie, etc.) comme des TS violentes. Dans les cohortes naturelles de suicidants, les TS par IMV sont les plus fréquentes (80 à 95% de cas) (55,56). Cependant, l'utilisation d'une méthode violente comme la pendaison serait associée à un risque plus élevé de décès ultérieur par suicide (55,57).

Les TS sont dites *hautement létales* ou *sérieuses* (*serious attempts*) si elles nécessitent une hospitalisation en médecine au décours ou si elles auraient été fatales sans l'apport d'un traitement d'urgence rapide et efficace. Un antécédent de TS sérieuse serait également associé à des taux élevés de décès par suicide (58).

### g. Le parasuicide

En 1969, Kreitman introduit le terme de « parasuicide » qui sera défini comme : « Un acte dont l'issue n'est pas fatale, dans lequel un individu initie délibérément un comportement non habituel qui, sans l'intervention d'autrui, provoquera une automutilation, ou ingère délibérément une substance au-delà de la dose thérapeutique prescrite ou généralement

reconnue, et qui vise à réaliser les changements que le sujet désire, par le biais des conséquences physiques réelles ou attendues » (40).

Ce terme a été utilisé dans la littérature scientifique pendant plusieurs années et de différentes manières, avant d'être finalement abandonné (59):

- Le parasuicide était considéré comme une sous-catégorie de TS caractérisée par un faible niveau d'intention de mourir. Cette définition est utilisée en Amérique.
- La TS est une sous-catégorie plus spécifique du parasuicide caractérisée par une forte intention de mourir. Cette perspective est privilégiée en Europe.
- Le parasuicide et la TS s'excluent mutuellement, le premier décrivant des cas à faible intention suicidaire, et le second étant utilisé pour désigner des cas où l'intention de mourir est clairement évidente.
- Le parasuicide et la TS sont utilisés de manière interchangeable, reconnaissant les difficultés inhérentes à la détermination de l'intention.

### h. Les passages à l'acte auto-agressifs

Le terme de *passage à l'acte auto-agressif (PAA)* ou *deliberate self-harm (DSH)* est utilisé plus particulièrement au Royaume-Uni, Afrique du Sud, Australie et Nouvelle Zélande pour désigner à la fois les lésions auto-infligées non suicidaires et les TS. Devant la difficulté à évaluer l'intentionnalité suicidaire d'un automutilation, certains auteurs ont suggéré d'inclure dans les TS toutes les automutilations (40,46). Néanmoins, cette définition néglige l'association entre l'intentionnalité suicidaire et le risque de décès par suicide (40,60).

### i. Les suicidants

Les sujets survivant à une TS sont appelés *suicidants*. Ils sont considérés comme des *primo-suicidants* s'il s'agit de leur première TS. Dans une cohorte naturelle de suicidants, la moitié sont des primo-suicidants (27,61,62). Comme nous l'avons abordé précédemment, l'antécédent de TS est un des principaux facteurs de risque de décès par suicide (23,24). Le taux de décès par suicide est le plus important dans l'année suivant une TS ; avec un taux qui varie dans les études entre 1.4% et 4.4% (63–67). Les suicidants constituent donc un sous-groupe de patients particulièrement à risque de récidiver une TS et de décéder par suicide. On estime que l'espérance de vie des suicidants est réduite de 8 à 18 ans selon le sexe et l'âge de survenue de la première TS (24). Plusieurs facteurs semblent être impliqués dans le décès par suicide chez les suicidants. A l'heure actuelle, un antécédent de TS violente (pendaison,

étranglement, suffocation, saut d'un lieu en hauteur), souffrir d'un trouble psychiatrique sévère et la répétition des tentatives sont les principaux facteurs de risque de décès par suicide qui ont été identifiés (68,69). De plus, la période la plus à risque de récidive serait les six premiers mois après la TS.

Premièrement, les études qui ont recherché des facteurs de risque de récidive de TS l'ont réalisé à l'aide des approches statistiques usuelles qui mettent en avant le lien entre un seul facteur de risque individuel ou environnemental et la récidive. Néanmoins, dans une revue de littérature en 2020, Fazel suggère que le risque suicidaire ne doit pas se limiter à la présence d'un seul facteur de risque mais correspondrait plutôt à l'interaction de différents facteurs intervenant tout au long de la vie, de la vie anténatale à l'âge adulte (23). Par ailleurs, alors que les traitements psychotropes sont largement prescrits après une TS, peu d'études ont analysé l'impact de ces prescriptions sur la récidive de TS. Pourtant, connaître l'impact positif ou négatif de traitements largement prescrits sur la récidive suicidaire paraît très important si l'on souhaite diminuer ce risque. En résumé, la recherche d'interactions entre les facteurs de risque et la recherche de l'impact des psychotropes sur la récidive de TS sont deux approches innovantes qui permettraient de mettre en évidence d'un côté des groupes de patients à risque de récidive et d'un autre côté l'impact des traitements prescrits sur ces patients.

Deuxièmement, alors que l'espérance de vie des suicidants est fortement réduite, leur devenir en termes de moralité n'est pas clair. En effet, plusieurs études se sont intéressées au devenir des patients ayant fait un passage à l'acte auto-agressif, peu de travaux ont tenté de déterminer les causes de décès chez les patients ayant fait une TS et les facteurs de risque de décès prématuré (70–72). Or, le taux de mortalité et les causes de décès ne sont probablement pas les mêmes après une TS ou après n'importe quel passage à l'acte auto-agressif. Ensuite, les travaux qui ont essayé de déterminer les causes de décès chez les patients suicidants ont souvent utilisés les registres nationaux de mortalité et se sont heurtés à des taux élevés de causes inconnues de décès (24,56,73).

Parmi les patients souffrant de troubles psychiatriques, les suicidants apparaissent donc comme étant un groupe de patients dont l'espérance de vie est fortement réduite en lien avec une morbi-mortalité par TS et suicide qui est importante. Par conséquent, plusieurs dispositifs de prévention ont été développés spécifiquement autour de la prévention du suicide chez les suicidants (74). Parmi les dispositifs spécifiques de prévention du suicide chez les suicidants, des dispositifs de re-contact téléphonique ont été développés ces dernières années (75,76). Malgré les travaux autour des dispositifs de prévention, les taux de récidive suicidaire restent

encore élevés. Améliorer ces outils de prévention à l'aide d'études épidémiologiques est crucial si l'on souhaite diminuer la morbi-mortalité par TS et suicide. De nouvelles études épidémiologiques pourraient identifier des sous-groupes de patients parmi les suicidants les plus à risque de récidiver afin de personnaliser l'intervention qui est réalisée. Enfin, l'amélioration des dispositifs de prévention passe également par l'évaluation de leur efficacité. Il est en effet essentiel de déterminer si les programmes de prévention du suicide sont efficaces pour réduire les taux de suicide et de TS afin d'optimiser leur utilisation.

Dans la suite de ce travail nous allons nous intéresser tout particulièrement à la morbi-mortalité des suicidants. Ce travail de thèse comportera trois parties successives autour de la morbidité par TS et la mortalité par suicide chez les suicidants et l'évaluation de dispositifs de prévention afin d'améliorer les connaissances en épidémiologie et dans l'évaluation des dispositifs de prévention du suicide. Ainsi, les objectifs principaux des études présentées seront 1) d'appréhender de nouveaux sous-groupes de patients à risque de récidive de TS à l'aide d'approches innovantes, 2) de déterminer le devenir des suicidants en termes de mortalité avec l'estimation du taux de mortalité, des causes et des facteurs de risque associés, 3) donner un exemple d'évaluation d'un dispositif de prévention du suicide qui a consisté en la formation d'agents sentinelles dans les maisons de retraite.

Dans la première partie de ce travail, nous tenterons de mettre en évidence les facteurs de risque sociodémographique, cliniques et thérapeutiques de récidive de TS, dans l'année suivant une TS, de manière innovante. Premièrement, nous allons mettre en évidence des sous-groupes de patients les plus à risque de récidive de TS parmi les suicidants. Pour cela, une interaction entre des facteurs de risque sociodémographiques et cliniques sera recherchée à l'aide d'approches statistiques innovantes issues des méthodes informatiques tel que les arbres de survie. Enfin, un algorithme simple de prédiction du risque de récidive sera disponible pour le clinicien et facilitera l'orientation des patients suicidants. Deuxièmement, nous réaliseront une étude pharmaco-épidémiologique pour évaluer l'impact des prescriptions de psychotropes sur les personnes ayant fait une TS. Nous nous appuierons pour ceux deux études sur la cohorte multicentrique ALGOS constituée de patients consultant aux urgences après une TS. Identifier des facteurs de risque de récidive avec des outils statistiques innovants tels que les arbres de survie et les analyses pharmaco-épidémiologiques permettrait d'améliorer l'évaluation clinique de ces patients, leur prise en charge thérapeutique et d'améliorer les outils de prévention en développant des interventions spécifiques pour les sous-groupes les plus à risque.

Ensuite, la deuxième partie s'intéressera au devenir des suicidants en termes de mortalité. Comme nous l'avons mentionné plus haut, les suicidant ont une espérance de vie fortement réduite et peu d'études ont évalué le taux et les causes de décès chez les suicidants. Toutefois, la mortalité par suicide a été la plus étudiée mais dans des contextes cliniques différents. Dans un premier temps, nous avons donc estimé le taux de mortalité par suicide à 1, 5 et 10 ans après une TS à l'aide d'une revue de la littérature scientifique et une méta-analyse. Nous avons inclus les études quel que soit la pathologie psychiatrique, l'âge ou le lieu d'inclusion des suicidants. Dans un second temps, nous avons tenté de mettre en évidence le taux de mortalité, les causes de mortalité et les facteurs de risque de décès dans l'année suivant une TS à l'aide d'une grande cohorte de patients suicidants issus du dispositif VigilanS de re-contact téléphonique des suicidants.

Enfin, la dernière partie de ce travail porte sur l'évaluation d'un dispositif de prévention du suicide. Évaluer les dispositifs existants de prévention du suicide est essentiel si l'on souhaite améliorer les pratiques et poursuivre notre objectif de baisse du taux de suicide. Nous prendrons l'exemple de la formation Terra Séguin qui a consisté en la formation de sentinelles dans les maisons de retraite de 2016 à 2018 dans les Hauts-de-France. La formation d'agents sentinelles dans les maisons de retraite semble particulièrement importante étant donné le taux élevé de décès par suicide chez les personnes âgées. Pour appréhender l'efficacité de ce programme de prévention, nous évaluerons les connaissances et les représentations sur le suicide à l'issue de la formation puis nous comparerons la morbi-mortalité par TS et suicide avant et après la formation.

Les trois parties de cette thèse s'articuleront autour de cinq travaux publiés dans des revues scientifiques internationales. Les deux premières parties permettront d'améliorer les connaissances sur le devenir des patients suicidants en termes de morbi-mortalité. L'utilisation de différents outils statistiques, dans deux grandes cohortes de patients suicidants et la réalisation d'une méta-analyse de la littérature scientifique a permis de mettre en évidence les taux de récidive et de décès et des sous-populations à risque de récidive et de décès. Enfin, la troisième partie est un exemple d'évaluation d'un dispositif innovant de prévention du suicide. Cet outil a été développé dans une population au taux élevé de décès par suicide et permet de discuter de la complexité de l'évaluation des outils de prévention existants.

# I. ANALYSE DE LA MORBIDITE APRES UNE TENTATIVE DE SUICIDE

La première partie de ce travail nous nous sommes intéressés à rechercher de facteurs de risque de récidive de TS chez les suicidants. En effet, comme nous l'avons évoqué plus haut, les suicidants constituent une population à haut risque de récidive suicidaire et de décès par suicide (23,24). Dans ce contexte, la recherche de facteurs de risque sociodémographiques, cliniques et médicamenteux de récidive de TS nous paraît particulièrement importante. De plus, l'utilisation d'outils statistiques innovants tels que les arbres de survie et les analyses pharmaco-épidémiologiques permettraient d'améliorer les connaissances actuelles de manière originale.

Les deux travaux que nous allons vous présenter dans ce chapitre se sont appuyés sur les données de l'étude ALGOS qui visait à montrer l'efficacité d'un dispositif de veille post-hospitalière des suicidants sur la récidive de TS (62). Nous allons donc débuter ce chapitre par une exposition de l'étude ALGOS suivi d'une présentation des deux études réalisées.

## 1. Présentation de l'étude ALGOS

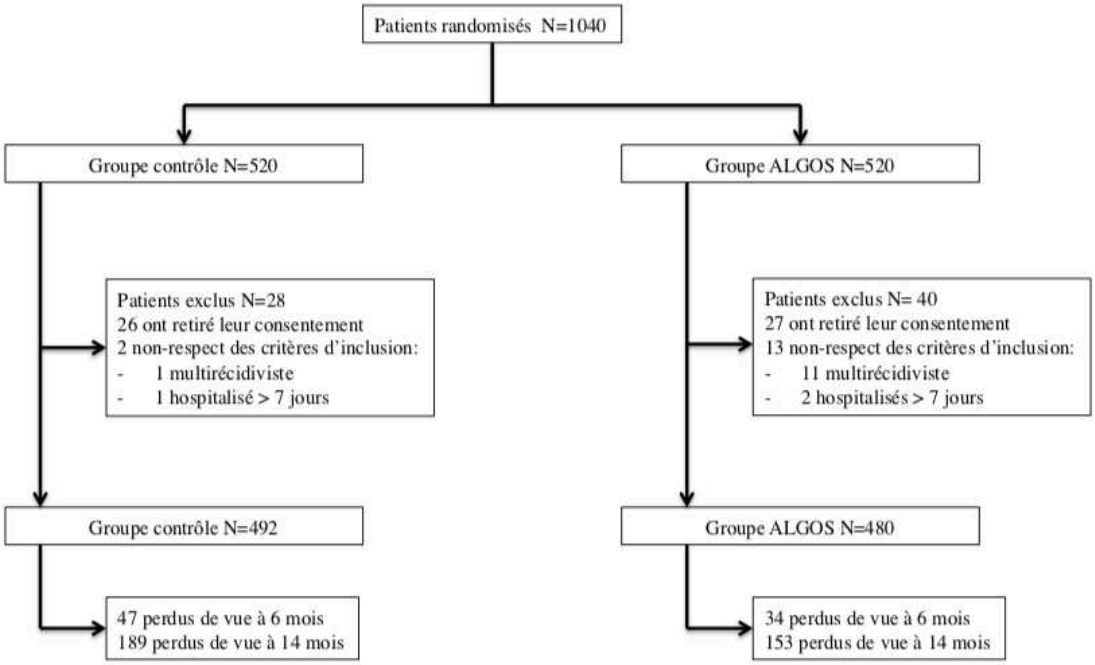
L'étude ALGOS est un essai clinique multicentrique, prospectif, en simple aveugle, randomisé avec deux groupes parallèles. L'essai a été conduit de janvier 2010 à février 2013 dans 23 services des urgences en France (CHU Angers, CHU de Brest, CHU de Caen, CHU de Clermont Ferrand, CHU de Créteil Henri Mondor, CHU de Lille, CHU de Marseille, CHU de Montpellier, CHU de Nancy, CHU de Nantes, CHU de Nice, CHU de Paris HEGP, CHU de Rennes, CHU de Toulouse, CH de Boulogne, CH de Douai, CH de Dunkerque, Polyclinique d'Henin Beaumont, CH de Montauban, CH de Quimper, CH de Roubaix, CH de Tourcoing, CH de Vannes) .

Le PHRC ALGOS a été autorisé par l'AFFSAPS (numéro NCT01123174) et a été approuvé par le Comité de Protection des Personnes de la région Nord-Ouest (décision CPP Nord-Ouest 09/63). Les participants ont donné leur consentement libre, éclairé et signé.

Les 972 participants ont été inclus aux urgences par des médecins urgentistes dans les 7 jours après une TS et ont été suivis pendant une durée de 14 mois. Les participants ont été assignés dans le groupe intervention qui bénéficiait du dispositif de veille post-hospitalière selon l'algorithme ALGOS ou dans le groupe témoin qui ne bénéficiait pas du dispositif de veille (cf. **Figure 1**).

Les critères d'inclusion étaient : des hommes et femmes, âgés de plus de 18 ans, ayant survécu à une TS et ce quel que soit le mode de TS. Les critères de non-inclusion étaient les patients mineurs et ceux ayant fait plus de 4 TS dans les 3 dernières années.

Figure 1. Diagramme de flux de l'étude ALGOS




L'algorithme ALGOS s'est déployé comme suit pour le groupe intervention :

- Les primo-suicidants ont bénéficié de la remise d'une « carte de crise » avec les numéros de téléphone des services d'urgences du centre d'inclusion
- Les patients non primo-suicidants ont reçu un appel téléphonique, entre le 10e et 21e jour après la TS, par un psychologue formé du CHU de Lille. Celui-ci relevait 3 situations possibles : soit la situation de crise s'était améliorée, soit le participant était en difficulté ou non compliant, et enfin le participant était à risque élevé de suicide

Les secours (SAMU/Centre 15) ont été appelés pour les participants à risque élevé de suicide. Les participants en difficulté ou ceux à risque élevé de suicide ont bénéficié de l'envoi de cartes postales au 2e, 3e, 4e et 5e mois après la TS avec les numéros du service de permanence des soins du centre d'inclusion.

Tous les participants ont bénéficié d'un entretien téléphonique à l'inclusion, à 6 mois et à 14 mois. Lors de cet entretien téléphonique, les caractéristiques sociodémographiques (l'âge, le sexe, la situation familiale et professionnelle), le nombre de TS antérieures, la méthode de TS, un mini-MINI et des items sélectionnés de l'échelle d'intentionnalité suicidaire de Beck ont été recueillis pour tous les participants à l'inclusion. Ensuite, lors de l'entretien téléphonique à 6 et à 14 mois, les psychotropes consommés par les patients depuis l'inclusion, une échelle psychiatriques standardisée (*Mini International Neuropsychiatric Interview* (MINI)(77)), une évaluation médico-économique (reprenant la méthode validée de Beecham et Knapp (78)), le nombre de récidives suicidaires et la date de la première récidive ont été recueillis.

Malgré un plus faible taux de récidive de TS dans le groupe bénéficiant du dispositif de veille (12,8% contre 17,2% dans le groupe contrôle), cet essai clinique conclut à une absence de différence en termes de récidive suicidaire pour les deux groupes (p=0.059).

## 2. Identification de sous-groupes de patients à haut risque de récidive

Le premier article de cette thèse s'intéresse aux facteurs de risque de récidive de TS chez les suicidants. Plusieurs facteurs de risque ont été mis en évidence dans la littérature comme le fait de souffrir d'un trouble psychiatrique sévère, avoir un antécédent de TS violente etc. Toutefois, ces études ont recherché l'effet d'un seul facteur de risque sur la récidive. Nous avons essayé de mettre en évidence dans notre travail des interactions entre les facteurs sociodémographiques et clinique qui permettent d'augmenter ou de diminuer le risque de récidive, dans les 6 mois après la TS, afin de proposer au clinicien un outil simple de prédiction du risque suicidaire. Les 6 premiers mois après la TS étant la période la plus à risque de récidive.

Notre étude s'appuie sur les données des patients inclus dans l'étude ALGOS. Cette étude a permis de constituer une cohorte de 972 sujets suicidants qui ont été suivis de manière prospective pendant 6 mois. Nous avons utilisé une méthode de fouille de données issue des science informatiques : un arbre de survie.

Les principaux résultats de notre étude montrent trois sous-groupes de patients suicidants à haut risque de récidive dans les 6 mois après une TS :

- Ceux ayant un trouble de l'usage d'alcool et ayant consommé de l'alcool lors de leur précédente TS
- Les patients avec un trouble anxieux
- Ceux ayant fait plus de 2 TS

Les participants qui n'avaient pas consommé d'alcool lors de leur précédente TS, qui ne souffraient pas de trouble anxieux et qui avaient fait moins de 2 TS constituaient le groupe de bon pronostic.

Article 1. Facteurs de risque de récidive de tentative et de suicide dans les 6 mois après une tentative dans la cohorte ALGOS : une analyse par arbre de survie

Cet article a été publié dans le Journal of Clinical Psychiatry en février 2021.


# Risk Factors for Reattempt and Suicide Within 6 Months After an Attempt in the French ALGOS Cohort: A Survival Tree Analysis

Alice Demesmaeker, MD, MSc[a,*]; Emmanuel Chazard, MD, PhD[b]; Guillaume Vaiva, MD, PhD[a,c]; and Ali Amad, MD, PhD[a]

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# Risk factors for re-attempt and suicide within 6 months after an attempt in the French ALGOS cohort: a survival tree analysis.

Alice DEMESMAEKER[1*] (MD), Emmanuel CHAZARD[2] (MD, PhD), Guillaume VAIVA[1,3] (MD, PhD), Ali AMAD[1](MD, PhD)

1) Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, F-59000 Lille, France
2) Univ. Lille, CHU Lille, ULR 2694, CERIM, Public health dept, F-59000 Lille, France
3) Centre national de ressources et de résilience (CN2R), F-59000 Lille, France

***Corresponding Author***

Dr Alice DEMESMAEKER (MD, PhD)

Hôpital Fontan, CHU de Lille, F-59037, Lille cedex, France

**Email:** alice.demesmaeker@chru-lille.fr

**Tel:** + 33 3 20 44 42 15 **Fax:** +33 3 20 44 62 65

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## ABSTRACT

INTRODUCTION: Understanding the cumulative effect of several risk factors involved in suicidal behavior is crucial for the development of effective prevention plans. The objective of this study is to provide clinicians with a simple predictive model of the risk of suicide attempts (SAs) and suicide within 6 months after SA.

METHOD: A prospective observational cohort of 972 subjects, included from January 26, 2010, to February 28, 2013, was used to perform a survival tree analysis with all sociodemographic and clinical variables available at inclusion. Then, the results of the decision tree were used to define a simple predictive algorithm for clinicians.

RESULTS: The results of survival tree analysis highlighted three subgroups of patients with an increased risk of SA or death by suicide within 6 months after SA: patients with alcohol use disorder and a previous SA with acute alcohol use (risk ratio (RR) 2.92 95% confidence interval [2.08 to 4.10]), patients with anxiety disorders (RR 0.98 [0.69 to 1.39]), or patients with a history of more than 2 SAs in the past 3 years (RR 2.11 [1.25 to 3.54]). The good prognosis group comprised all other patients.

CONCLUSION: By using a data-driven method, we identified four clinical factors interacting together to reduce or increase the risk of recidivism. These combinations of risk factors allow for a better evaluation of a subject's suicide risk in clinical practice.

TRIAL REGISTRATION: The ALGOS study was registered in ClinicalTrials.gov (NCT01123174).



Keywords: suicide, suicide attempt, risk factor, alcohol use disorder

# INTRODUCTION

With approximately 800,000 deaths by suicide throughout the world every year, including 10,000 in France, preventing suicide is a major public health issue [1]. In 2013, the World Health Assembly adopted the first-ever Mental Health Action Plan of the World Health Organization (WHO) [2]. This plan aims to reduce the rates of suicide by 10% from 2020. Nonetheless, worldwide suicide rates have been declining over recent decades except in the United States [3]. For example, the standardized mortality rate in France has decreased from 16.86 per 100,000 inhabitants in 2011 to 13.21 per 100,000 inhabitants in 2016 according to the national French death register "CépiDc" [4].

The understanding of risk factors involved in suicidal behavior is crucial for the development of effective prevention plans. Interestingly, one of the most robust risk factors for death by suicide corresponds to a history of previous suicide attempts (SAs) [5–7], as a substantial number of patients who attempt suicide ultimately die by suicide. According to a recent systematic review and meta-analysis, the pooled estimated incidence rate of subsequent fatal self-harm after an index attempt was relatively high at 1 year (1.6%) and even higher at 10 years (4.2%) [8]. Moreover, a recent exhaustive study of two national French registers including 45 million inhabitants highlighted that 1 year after SA, 2.6% of the subjects had died, 34.4% of them by suicide [9]. According to this study, the period of greatest risk of death by suicide corresponds to the first six months after SA. In addition, if a previous SA is a risk factor for subsequent suicide, SA is also a strong predictor for suicide re-attempt. For instance, after 1 year, nonfatal repetition rates are approximately 15% [10]. Similar results were found in France, with a recurrence of SA estimated at 12% within the first year after nonfatal self-harm, with the vast majority of recurrence of SA occurring within the first 6 months (75%)[9].

Beyond the risk related to a previous SA, several other factors seem to be involved in death by suicide in patients with a history of self-harm. In a cohort study defined from Danish registers, it has been shown that individuals who jumped from a high place or in front of traffic form a high-risk group for suicide [7]. Another Danish cohort study highlighted that age over 35 years, as well as hanging, strangling or suffocation as the method of the index attempt or receiving psychiatric hospitalization for this attempt, were also risk factors for future suicide [11]. Finally, the exploration of Swedish registers demonstrated that suffering from severe mental illness such as bipolar or psychotic disorder and a previous attempt by hanging were the most important risk factors for subsequent suicide [12].

To summarize, repetition of SA, the use of a violent method for a previous SA (jumping from a high place or in front of traffic, hanging, strangling and suffocation) and a severe mental

illness are the main factors involved in death by suicide according to different national registers. Moreover, the first six months after SA seem to be a particularly high-risk period for re-attempt and subsequent suicide.

Interestingly, it has been suggested that a subject's suicide risk was not limited to one event but would rather correspond to the interplay of different factors occurring throughout life from pre-birth (e.g., low birth weight and genetic predisposition) to adulthood (socioeconomic factors, severe mental illness, substance abuse) [1]. In the same way, it has recently been indicated that the lifetime cumulative effect of several risk factors should be considered instead of individual risk factors for suicide being examined [3].

While the current scientific literature can determine the extent to which an individual or environmental factor increases the risk of SA or death by suicide through the use of conventional statistical methods, the published results encounter many drawbacks. The methods employed rarely produce simple tools that can be used by clinicians and hardly explore the interactions between variables [3]. Interestingly, flexible data-mining methods derived from computer science, such as survival trees, have been developed to detect interactions among variables that best explain a time-dependent variable of interest by means of recursive partitioning [13]. The objective of this study is to provide clinicians with a simple predictive model of the risk of SA and suicide within 6 months after SA.

# METHOD

## Study Design

A prospective observational cohort of 972 subjects from the ALGOS study was used for the analysis. The ALGOS study is a multicentric, prospective, single-blind, randomized and controlled clinical trial with two parallel groups conducted from January 26, 2010, to February 28, 2013. Participants in the intervention group received a brief contact intervention for 6 months [14], and control participants did not receive any intervention. Both groups were used in the present study. This study was conducted in 23 French emergency services. After inclusion by an emergency physician, the ALGOS algorithm combines brief contact interventions such as the delivery of a crisis card (with emergency department phone number) for the first attempts and a telephone contact between the 10th and 21st day after SA for those with previous attempts. Handwritten postcards were also sent at months 2, 3, 4, and 5 to patients with previous SAs who were not available for a phone call or experiencing a suicidal crisis. These interventions were conducted by a team of trained psychologists from the University Hospital of Lille. Patients included were men and women of legal age who survived an SA in the 7 days prior to inclusion, regardless of the method used for the SA. Patients who had no suicidal intent, were homeless, were under guardianship, or were multirepeaters (more than 4 SAs in the last 3 years) were excluded from the study. Multi-repeaters were excluded from this trial as a lower impact of the brief contact interventions has been demonstrated for these subjects[15]. Further details are available in the initial trial[16]. All participants of the ALGOS study provided signed consent.

This study has received authorization from AFFSAPS (number NCT01123174) and has been approved by the Committee for the Protection of Persons in the North-West Region (CPP North-West decision 09/63). The ALGOS study was registered in ClinicalTrials.gov (NCT01123174).

## Collected data

At inclusion, data on sociodemographic characteristics (age, gender, family and work status), number of previous SAs and method of SA (drug overdose, acute alcohol use), as well as responses to a questionnaire based on Beck's intentionality scale, were collected for all subjects. This questionnaire explored the circumstances related to the SA (expression of suicidal ideations, suicidal project, testamentary precautions, suicide note), predisposing factors (family history of mental illness, chronic pain, chronic medical condition, social isolation) and precipitating factors (self-medication, poor adherence to treatment, negative life events). All

participants were also assessed by using screening question(s) from the MINI (Mini International Neuropsychiatric Interview) corresponding to the main criteria for major depressive disorder, anxiety disorder (generalized anxiety disorder or panic disorder), alcohol use disorder (AUD) and eating disorder [17].

At 6 months, the number of suicidal recurrences and the date of the first recurrence were evaluated for all participants through a standardized telephone interview by trained psychologists.

## Statistical analysis

### Descriptive analyses

Descriptive statistics were calculated for the variables of interest. Continuous variables are presented as the means and standard deviations (SDs). Asymmetric distributions are reported with the median and the first and third quartiles (Q1-Q3). The 95% confidence intervals (95% CIs) were calculated using the central limit theorem. Discrete variables are expressed as frequencies and percentages.

### Automated risk prediction

To explain the risk of suicide re-attempt within 6 months after an index SA, we performed a survival tree with all the variables available at inclusion (age, gender, family and work status, randomization group (ALGOS or control group), number of previous SAs, suicidal method used for the index SA, acute alcohol use during index SA) and clinical data. Survival trees are predictive data mining and decision support tools allowing us to obtain homogeneous classes of individuals with regard to the time-dependent variable of interest, based on recursive partitioning, by handling interactions between covariates [13]. Then, survival curves estimated by the Kaplan-Meier method were drawn corresponding to the leaves of the tree. Tree performance was assessed through a ROC curve and area-under-the-curve (AUC) estimation.

### Predictive algorithm for clinicians

Finally, the results of the decision tree were used to define a simple predictive algorithm for clinicians. Kaplan-Meier curves were also drawn, and the AUC was computed. The hazard ratio and its 95% CI were computed using a Cox model.

Only complete cases were analyzed. Tests were 2-sided, and p values were considered significant under 0.05. The Rpart package from R software version 3.6.1 was used for the analysis [18].

# RESULTS

A total of 972 participants were included (cf. Table 1). Regarding the number of previous SAs, more than half of the patients were first-time attempters (53.3%). In addition, a high proportion of patients suffered from major depressive disorder and anxiety disorder (42.6% and 47.2%, respectively) at inclusion.

For 880 participants (90.5%), the complete status at 6 months was known. Of these patients, 117 (13.3%) had repeated SAs, 11 (1.1%) of whom completed suicide. On those who completed suicide, 6 were females, 8 were non-first-time attempters, 9 were randomized in control group and most of them were suffering from major depressive disorder (7 participants) or anxiety disorder (9 participants). Ninety-two patients (9.5%) were lost to follow-up at 6 months (47 women and 45 men). Fifty-two (56.5%) of them were between 26 and 50 years old, and 53 (57.6%) were first attempters.

*Insert Table 1 about here.*

## Automated risk prediction

Of the 878 (90.3%) patients, complete cases (i.e., the root node of the tree) that were used for the analysis, 115 (13.1%) had repeated SAs (see Figure 1). The CART (Classification and regression trees) algorithm highlighted five leaves (i.e., defining subgroups), among which three present an increased risk of SA or suicide.

The first subgroup (leaf N°1, Figure 1) was composed of 361 individuals without AUD, with less than 2 previous SAs in the past 3 years and without anxiety disorder. Twenty-three of these participants repeated SA in the six months. The relative event rate (RER) compared to the root was 0.49, and the risk ratio (RR with 95% CI) was 0.36 [0.23 to 0.55].

The next subgroup (leaf N°2, Figure 1) was composed of 325 individuals without AUD, with a history of 1 or 2 previous SAs in the past 3 years and anxiety disorder. Forty-two of those 325 subjects repeated SA in the 6 months. Suffering from an anxiety disorder (generalized anxiety or panic disorder) nonsignificantly increases the risk of SA and suicide for these patients, with an RER of 1 and an RR of 0.98 [0.69 to 1.39].

In the third leaf (leaf N°3, Figure 1) composed of 46 individuals without AUD and with a history of more than 2 SAs in the past 3 years, 12 individuals repeated SA. Furthermore, recurrence of SA was associated with an increased risk of SA re-attempt and suicide, the RER was equal to 2, and the RR was 2.11 [1.25 to 3.54].

The fourth subgroup (leaf N°4, Figure 1) was composed of 19 individuals with AUD and without acute alcohol use during their last SA. None of them repeated SA. Therefore, the RER was 0.28, and the RR was close to 0.

Finally, the last subgroup (leaf Nr 5 in Figure 1) was composed of individuals with AUD and acute alcohol use (AAU). Among those 127 patients, 38 (29.9%) repeated SA or died by suicide. The RER was 2.2 in regard to the root, and the RR was 2.92 [2.08 to 4.10].

The survival curves of each terminal leaf representing the time before the first recurrence of SA within 6 months, estimated by the Kaplan-Meier method, are rendered in Figure 2.

Predictive algorithm for clinicians

Based on the previous results, to provide clinicians with a simple predictive algorithm, we separated the patients into two groups of good or poor prognosis. The poor prognosis group is composed of participants with acute alcohol use during their last SA, with anxiety disorder, or with a history of more than 2 SAs in the past 3 years. The good prognosis group comprised all other patients. The survival curves with the confidence interval corresponding to the good and bad prognosis groups are rendered in Figure 3. The poor prognosis group appears to be a risk factor for SA re-attempt, with HR=1.78 [1.42 to 2.24] ($p<0.01$). This predictive algorithm obtains an AUC of 0.63. It renders a specificity of 0.47 [0.42 to 0.50], a sensitivity of 0.8 [0.73 to 0.87], a positive predictive value of 0.19 [0.15 to 0.22], and a negative predictive value of 0.94 [0.92 to 0.96].

*Insert Figures 1, 2 and 3 about here.*

# DISCUSSION

Through this study, a very simple algorithm of SA re-attempt or suicide was proposed. This algorithm was based on four simple clinical factors and still had good predictive power. Indeed, two groups of good or poor prognosis of suicide re-attempt were identified according to the sociodemographic or clinical elements collected after their previous SA. The poor prognosis group is composed of participants suffering from AUD with AAU during their last SA, those with anxiety disorders such as generalized anxiety or panic disorder, or those with a history of more than 2 SAs in the past 3 years. This predictive algorithm can be easily used by clinicians assessing patients who have attempted suicide to provide the most appropriate medical care.

The results of our survival tree analysis highlighted three subgroups of patients with an increased risk of SA or death by suicide within 6 months after SA. The first subgroup was composed of patients with an alcohol use disorder and a previous SA with acute alcohol use. Moreover, subjects with AUD for which previous SA was associated with an AAU had an even greater risk of suicide re-attempt (RER= 2.2), while those without AAU had a lower risk (RER= 0.28). Thus, AAU during the last SA appears to be a determining factor in the future prognosis. The second subgroup corresponds to patients with a history of more than 2 previous SAs in the past 3 years. Finally, the last subgroup is composed of patients with generalized anxiety or panic disorder, without AUD and with less than 2 previous SAs in the past 3 years. Therefore, the increased risk of SA or death by suicide is best explained by one of these conditions: AUD associated with acute alcohol use during the last SA, an anxiety disorder, and the recurrence of SA.

Interestingly, we used a survival tree to explore the possible interaction between a great number of sociodemographic or clinical variables. Although this method is rarely used in medical research, it allows us to identify the most relevant factors in a dataset without establishing a specific hypothesis and to study the association of different factors regarding a time variable of interest (i.e., the risk of suicide/re-attempt after SA). In contrast, traditional methods to analyze survival data are based on the Cox proportional hazard regression model to test a specific link between the covariates and the response. In this type of model, any interaction between variables must be specified beforehand.

Very few studies have focused on the association among risk factors using data-driven methods. Among decision trees, a regression tree was used in a study aiming to build a dynamic clinical decision-support system (CDSS) for suicide prevention in 2802 suicide attempters [19]. Compared to our results, the authors identified impulsivity aspects and some interactions of

factors that pose a particular risk of recidivism, such as eating disorders for women or a history of familial suicidal behavior and employment status for men. Another decision tree based on the CHAID algorithm (chi-square automatic interaction detection) of 2,754 middle and high schools also found different explanatory factors, such as the severity of depression, which seems to be the strongest variable predicting SA interacting with greater delinquency and lower family intimacy to increase the risk of SA [20]. In addition, a classification tree developed to predict a high risk of SA in 6,686 Chinese high school students indicated interactions among depression, anxiety, social support, gender, self-esteem, family cohesion and adaptability as predictors of high suicide attempt risk (e.g., female adolescents with low social support and low depression scores were at high risk of SA)[21]. Therefore, anxiety seems to be the only risk factor found in both of our studies. Finally, among 218 patients discharged from psychiatric hospitalization after an SA, a recursive partitioning classification tree highlighted that previous SA characteristics (such as definite plans or extensive preparation) posed a high risk of re-attempt[22]. In fact, studies investigating the interactions of factors to assess suicidal risk are rare. However, these emerging methods based on computer science have shown particularly good results to evaluate high-risk groups for suicide in a study comparing different statistical or computer-based methods [23].

Studies that have used more conventional methods (such as logistic regressions or Cox models) and that focus on few risk factors that are hypothesis-driven have often shown that certain factors are powerful in predicting suicide. According to our results, having an AUD or anxiety disorder (generalized anxiety or panic disorder) appears to be a determining factor in the prognosis after SA. Regarding psychiatric disorders, a meta-analysis obtained similar results. with an increased risk of suicide in patients with opioid use or women with alcohol use disorder [24]. In contrast, a more recent study found the highest rates of suicide in subjects with substance use disorder but also the lowest rates in those with anxiety disorders [25].

Our findings also indicate an interaction between AUD and a previous SA with acute alcohol use, thus increasing the risk for these patients. Nevertheless, a recent review on risk factors for SA and suicide in patients with substance use disorder did not show any interaction with acute alcohol use during last SA but did show an association with environmental factors (marital and interpersonal relationship disruption, occupational and financial stressors, recent heavy substance use) as well as a history of previous SA [26]. Similar results were found in the Australian Treatment Outcome Study among subjects suffering from heroin dependence, with high odds ratios for sociodemographic factors (female gender, younger age, less education) and acute substance use (polydrug use, benzodiazepine use and recent heroin overdose) [27].

Alcohol use disorder is a well-known risk factor for suicidal behavior [28]. Regarding AUD, a Korean study confirmed an increased risk of SA with a logistic regression for students who used alcohol daily (odds ratio (OR) = 8.00) [29]. Moreover, in a recent study using logistic regression, an increased risk of SA was associated alcohol-related deaths following self-harm in addition to unemployment, sickness or disabled status, among other factors; interestingly, SA was also associated with alcohol use during previous self-harm[30]. Conversely, our study also found a significant reduction in the risk of recurrence in patients suffering from AUD who had not consumed alcohol during their previous suicidal act. It could be suggested that a reduction or cessation of alcohol consumption or the medical management of the alcohol use disorder may decrease the risk of suicide behavior.

Additionally, statistical methods such as multivariate Cox regression models used to predict the risk of recidivism have also shown an increased risk in patients who have made at least one attempt in their lifetime [31.] Nevertheless, our method suggested an increased risk of re-attempt for patients with more than 2 SAs in the past 3 years, thus indicating the need to pay more attention to these patients.

Strengths and limitations

One of the strengths of our study is that among the large number of variables studied, a small number of factors are ultimately involved in suicide re-attempts and suicide and are brought to light by the CART method. The terminal nodes are clinically pertinent and based on simple combinations of medical risk factors. Moreover, the survival curve estimated by the Kaplan-Meier method corresponding to each terminal node showed very different prognoses depending on the subgroup to which they belonged. Another strength is the simple and intuitive nature of the CART algorithm, which allows for easy reading and captures much of the relevant covariate structure of the data.

One of the limits of this study is the relatively high number of patients lost to follow-up at 6 months (9.5%). Nonetheless, the ALGOS study was composed of a sufficient number of patients, and most of the patients lost to follow-up were younger than 60 years old and were first attempters and thus were at lower risk for SA and death by suicide. In addition, baseline assessment investigated only four psychiatric disorders from the MINI. However, focusing on these common disorders appears to be convenient in clinical practice, especially during a first psychiatric interview in an emergency room setting. Finally, alcohol use disorder is common in France and may affect a large proportion of the subjects in our study. This could be a limit to the extrapolation of our results to other parts of the world.

## CONCLUSION

In this study, we suggested that the medical history and the method used for the previous SA were the most important risk factors for suicidal behavior. Indeed, by using a data-driven method, we found that alcohol use disorder and acute alcohol consumption during the last SA were associated with an increase in the risk of recidivism, such as anxiety disorder and recurrence of SA. The absence of these factors allowed for a decrease in this risk, and then the interaction of these various factors contributes to reducing or increasing the risk of recidivism. To better understand the risk factors associated with suicide, we need to consider what happens with combinations of risk factors rather than examining them one by one or by using classical methods such as logistic regression. Suicide prevention should therefore also take place at several levels with better management of psychiatric disorders and increased secondary prevention of suicidal patients, with a focus on those with an alcohol use disorder.

## CLINICAL POINTS

- Flexible data-mining methods derived from computer science, such as survival trees, have been developed to detect interactions among risk factors of suicide re-attempt. Homogeneous subgroups of individuals are thus highlighted with simple clinical features.
- Three subgroups of patients presented with an increased risk of SA reattempt within 6 months after SA: patients with alcohol use disorder and a previous SA with acute alcohol use, patients with anxiety disorders, and patients with a history of more than 2 SAs in the past 3 years.
- Risk factors combinations highlighted by a data-driven method of risk factors allow for a better evaluation of a subject's suicide risk in clinical practice.

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***Table 1. Baseline Characteristics of Participants.***

| Characteristic | *All Patients N = 972 N (%)* |
|---|---|
| **Intervention group** | |
| ALGOS | 480 (49.4) |
| Control | 492 (50.6) |
| **Age** (mean ± SD: 38 ± 13.3) | |
| 18–35 y | 226 (23.3) |
| 36–55 y | 558 (57.4) |
| > 55 y | 188 (19.3) |
| **Women** | 618 (63.6) |
| **Men** | 354 (36.4) |
| **Living alone** | 515 (53.1) |
| **Employed** | 619 (63.9) |
| **First-attempters** | 518 (53.3) |
| **Lifetime diagnosis (per MINI)** | |
| Major depressive disorder | 412 (42.6) |
| GAD or Panic disorder | 455 (47.2) |
| Alcohol use disorder | 166 (17.2) |
| Eating disorder | 47 (4.9) |
| **Method of SA** | |
| SA by medication overdose | 912 (94) |
| SA with AAU | 417 (43.7) |
| **Circumstances related to the SA** | |
| Expression of suicidal ideations | 334 (34.7) |
| Suicidal project | 141 (14.6) |
| Testamentary precautions | 18 (1.9) |
| Suicide note | 125 (12.9) |
| **Predisposing factors** | |
| Family history of mental illness | 320 (35.7) |
| Chronic pain | 139 (14.4) |
| Chronic medical condition | 195 (20.1) |
| Social isolation | 197 (20.4) |
| **Precipitating factors** | |
| Self-medication | 189 (19.8) |
| Poor adherence to treatment | 172 (18.1) |
| Negative life events in the last 6 months | 616 (64.4) |

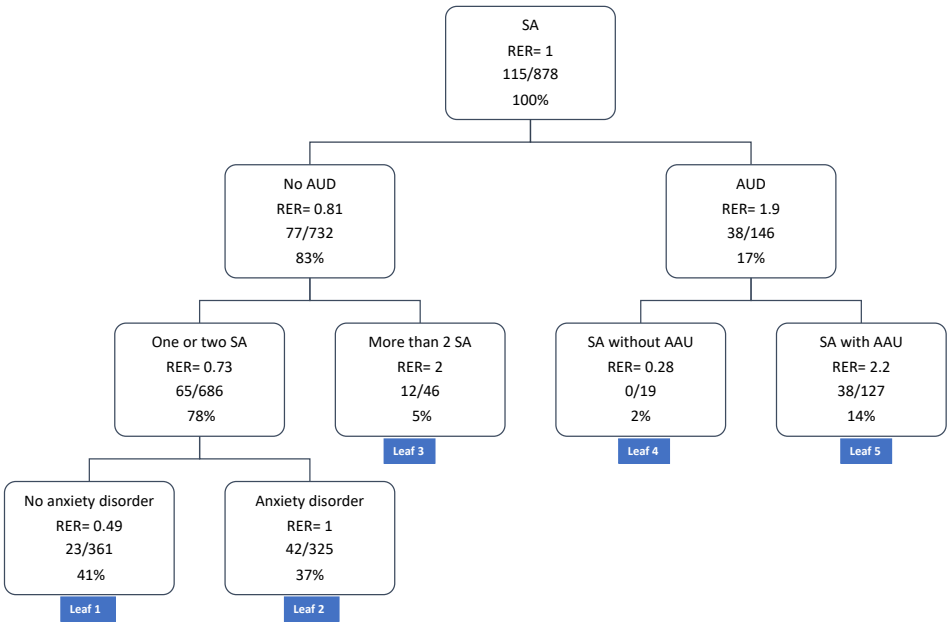
*Abbreviations:*

*AAU= acute alcohol use*

*GAD= generalized anxiety disorder*

*SA= suicide attempt*

***Figure 1. Survival tree for suicide re-attempt and suicide at 6 months after SA.***




*Abbreviations:*

*AUD= substance use disorder*

*AAU= acute alcohol use*

*RER= relative event rate compared to the root (proportion of events in the node on the proportion of events in the root)*

*SA= suicide attempt*

***Figure 2. Kaplan-Meier survival curves of the 5 terminal subgroups generated from the default CART analysis.*** *([1]Subjects with one or two previous SAs and no anxiety disorder; [2]Subjects with one or two previous SAs and an anxiety disorder; [3]Subjects with more than two previous SAs; [4]Subjects with AUD and a previous SA without acute alcohol use; [5]Subjects with AUD and a previous SA with acute alcohol use)*

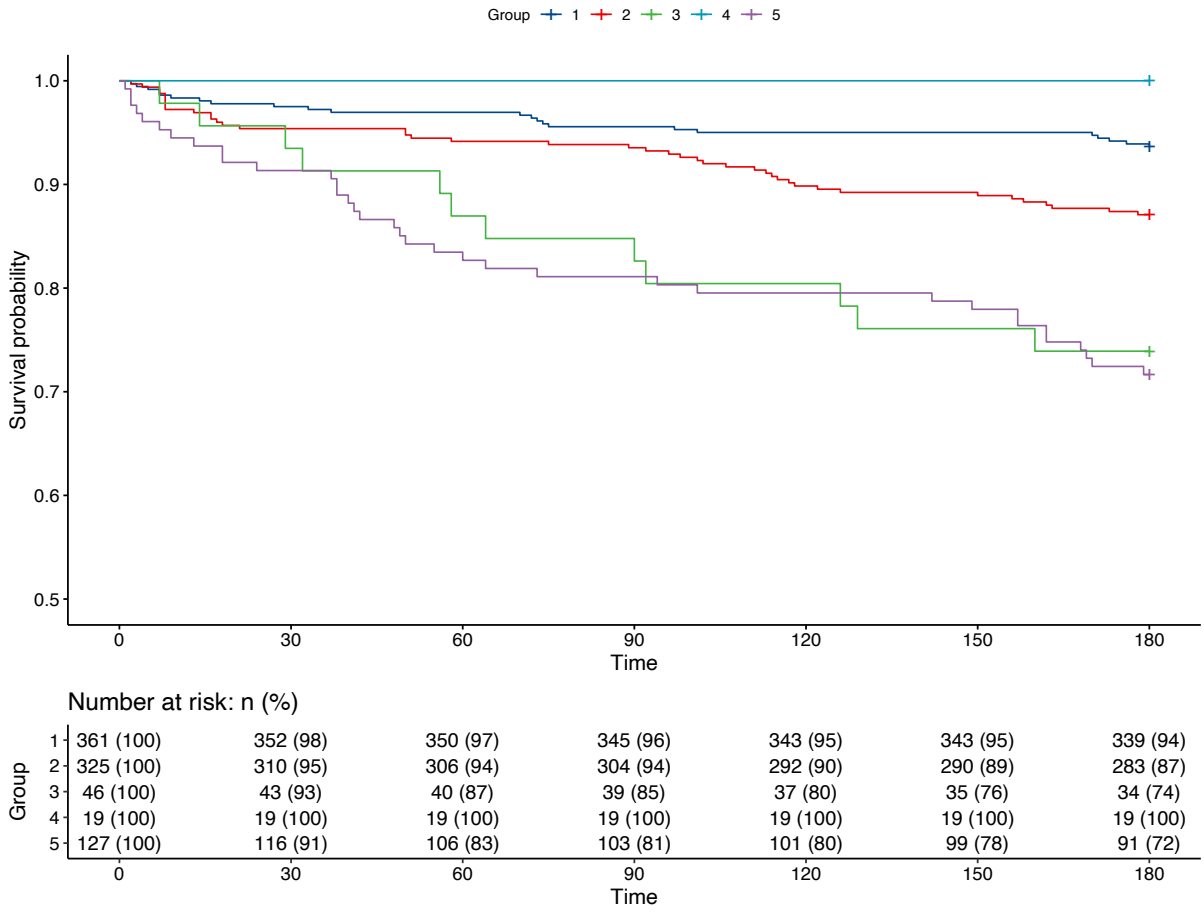
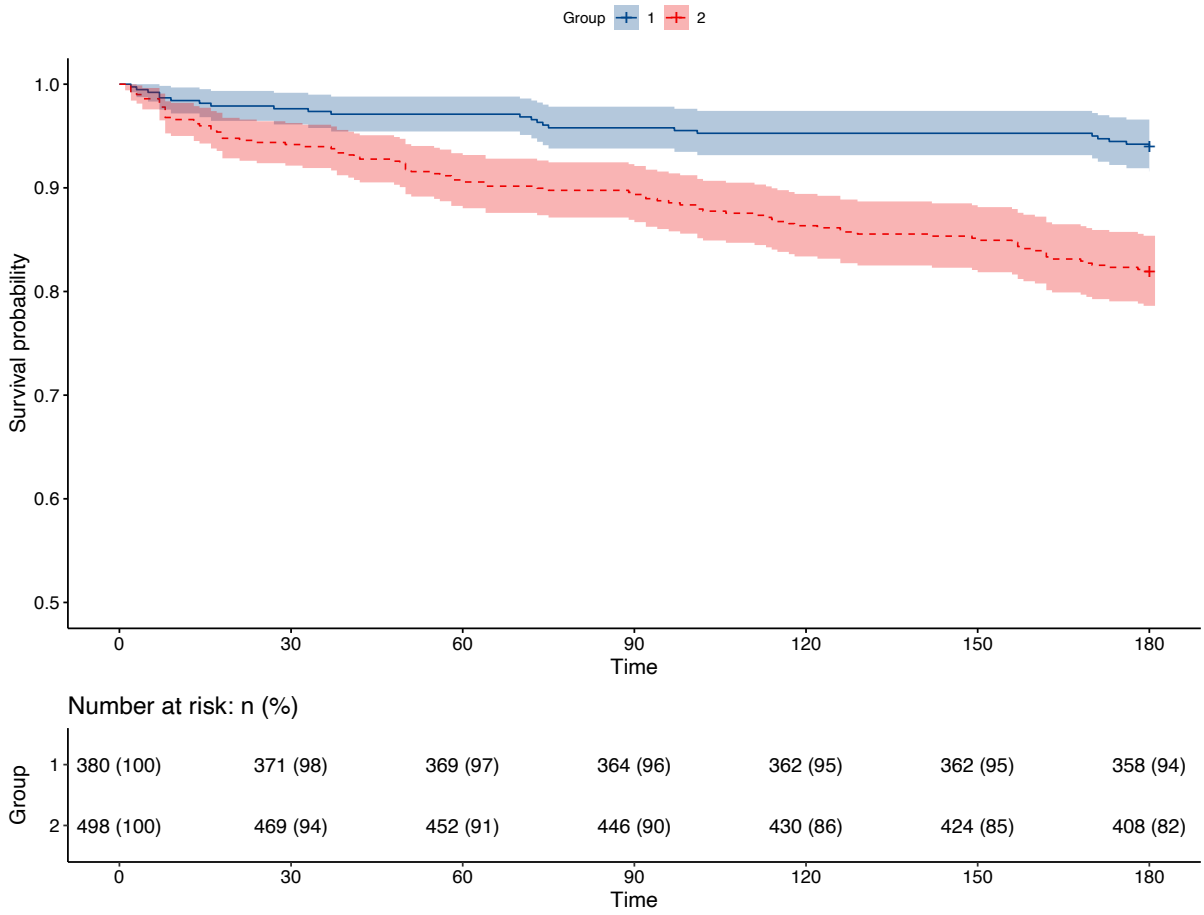


***Figure 3. Kaplan-Meier survival curves and confidence intervals of the terminal prognosis subgroups generated from the default CART analysis.*** *([1]Good prognosis group: Subjects with no acute alcohol use during last SA, one or two previous SA and no anxiety disorder; [2]Poor prognosis group: Subjects with acute alcohol use during last SA, more than 2 previous SA or an anxiety disorder; Log-rank test: p<0.01; Belonging to a poor prognosis group appears to be a risk factor in survival analysis (HR=1.78 [1.42 to 2.24])).*



## 3. Impact de la prescription de psychotropes sur le risque de récidive

Le deuxième travail de cette thèse est une étude pharmaco-épidémiologique qui recherche l'impact de la consommation de psychotropes sur le risque de récidive de TS dans les 6 et 14 mois après une TS.

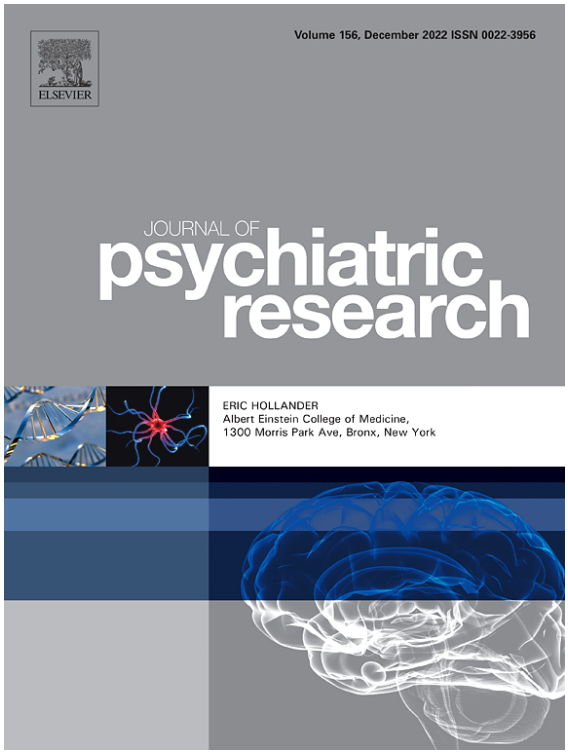
La littérature scientifique a mis en évidence un lien entre la consommation de psychotropes et les comportements suicidaires. Certains psychotropes sont ainsi apparus comme étant des facteurs de risque de TS et de suicide comme les antiépileptiques, certains antidépresseurs et les médicaments utilisés dans le sevrage tabagique. Au contraire, certains psychotropes ont été identifiés comme étant des facteurs protecteurs ; c'est le cas du lithium et de la clozapine chez les patients souffrant d'un trouble psychotique. Les suicidants sont une population à haut risque de récidive de TS et de décès par suicide. L'objectif de notre étude était de déterminer s'il y avait une association entre la consommation de psychotropes et la récidive de TS dans cette population.

Nous avons pour cela utilisé la cohorte prospective ALGOS constituée de 972 participants. Les traitements consommés par les participants étaient recueillis et une évaluation diagnostique était réalisée à l'aide d'un MINI à 6 et 14 mois. Nous avons utilisé un modèle de Cox afin d'identifier les associations entre les classes de psychotropes, les combinaisons de classes et l'adéquation entre la pathologie et le traitement, et le risque de récidive de TS à 6 et 14 mois.

Le résultat principal de notre étude est l'absence d'association entre les différentes classes de psychotropes et la récidive de TS à 6 mois. Cependant, on retrouvait une association entre la consommation de benzodiazépines, d'hypnotiques ou la combinaison des deux et le risque de récidive de TS à 14 mois ; avec un risque de récidive deux fois plus élevé pour ces patients. Une vigilance accrue semble donc nécessaire lorsque ces traitements sont prescrits.

## Article 2. Une étude pharmaco-épidémiologique de l'association entre l'exposition aux médicaments psychotropes et le risque de récidive suicide

Cette étude a été publiée dans le Journal of Psychiatric Research en avril 2021.




# A pharmacoepidemiological study of the association of suicide reattempt risk with psychotropic drug exposure

Alice Demesmaeker [a,*], Emmanuel Chazard [b], Guillaume Vaiva [a,c], Ali Amad [a]

[a] Univ. Lille, Inserm, CHU Lille, U1172, LilNCog - Lille Neuroscience & Cognition, F-59000, Lille, France
[b] Univ. Lille, CERIM, EA 2694- Santé publique et qualité des soins, F-59000, Lille, France
[c] Centre national de ressources et de résilience (CN2R), F-59000, Lille, France

# A pharmacoepidemiological study of the association of suicide reattempt risk with psychotropic drug exposure

Alice DEMESMAEKER[1*] (MD,MSC), Emmanuel CHAZARD[2] (MD, PhD), Guillaume VAIVA[1,3] (MD, PhD), Ali AMAD[1] (MD, PhD)

4) Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, F-59000 Lille, France
5) Univ. Lille, CERIM, EA 2694- Santé publique et qualité des soins, F-59000 Lille, France
6) Centre national de ressources et de résilience (CN2R), F-59000 Lille, France

***Corresponding Author***

Dr Alice DEMESMAEKER

Hôpital Fontan, CHU de Lille, F-59037, Lille cedex, France

**Email:** alice.demesmaeker@chu-lille.fr

**Tel:** + 33 3 20 44 42 15 **Fax:** +33 3 20 44 62 65

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Disclosures: The authors have no conflicts of interest to disclose

## ABSTRACT

INTRODUCTION: Recent pharmacoepidemiological studies have suggested that consumption of certain classes of psychotropic drugs could be considered protective or risk factors for suicidal behaviour. The aim of the study was to evaluate the association between the risk of suicide reattempt within 6 and 14 months after an suicide attempt (SA) with the use of different classes of psychotropic drugs, combination pairs and treatment adequacy from inclusion through 6 and 14 months post-SA.

METHOD: A prospective observational cohort of 972 subjects from the ALGOS study from January 2010 to February 2013 was used to evaluate the association of risk of suicide reattempt within 6 and 14 months with the use of different classes of psychotropic drugs (antidepressants, anxiolytics, antipsychotics, lithium, anticonvulsants, analgesics, opioid maintenance therapy and maintenance treatment for alcohol dependence). A multivariable Cox model was performed after imputation of missing data using the multiple imputation method.

RESULTS: Our main results did not show an association between psychotropic drug use and suicide reattempt after 6 months of follow-up. We demonstrated that the use of benzodiazepines (HR=1.87 [1.25; 2.81], p<0.01) and hypnotics (HR=1.49 [1.03; 2.17], p=0.04) or a combination of both (HR=1.80 [1.17; 2.72], p=0.01) were associated with suicide reattempt within 14 months after a previous SA.

CONCLUSION: The early identification of a positive association between psychotropic drugs and the risk of suicidal behaviour is extremely important for prevention of suicide reattempts. Special precautions should be considered when prescribing psychotropic drugs for these subjects, particularly those at risk of suicide reattempt.



Keywords: Suicide, suicide attempt, pharmacoepidemiology, psychotropic drug.


Key points:

- Certain classes of psychotropic drugs have already been considered potential protective or risk factors for suicidal behaviour
- Benzodiazepine and/or hypnotic consumption was associated with an increased risk of suicide reattempt within 14 months after a suicide attempt
- Special precautions be considered when prescribing benzodiazepines or hypnotics after a nonfatal suicide attempt.

# INTRODUCTION

For several decades, despite a decrease in the number of deaths, suicide has remained one of the leading causes of avoidable death worldwide, especially among individuals aged 15 to 24 years old (Fazel and Runeson, 2020). A high number of individuals present to health care services for suicide attempts (SAs) in France every year (Chan Chee and Jezewski Serra, 2014). Among patients who have previously self-harmed, 12.4% reattempted, and 2.6% died within a year (Vuagnat et al., 2019). According to various studies, the period with the highest risk of reattempt or death by suicide seems to be the first 6 months after an SA (Owens et al., 2002; Vuagnat et al., 2019).

Several study designs have been used to explore the associations between drugs and suicidal events, such as pharmacoepidemiologic studies evaluating drug use, effectiveness, risk of adverse effects and mortality in large populations (Thaker et al., 2015). Interestingly, it has been shown that patients who died by suicide were dispensed more psychotropic medications than the general population, including antidepressants, anxiolytics and hypnotics (Reneflot et al., 2019). The increasing number of psychotropic prescriptions before death by suicide can be easily explained by the increased severity of depression that may be experienced prior to dying by suicide. However, in recent years, pharmacoepidemiological studies have suggested that certain classes of drugs may have effects on suicidal behaviour and can thus be considered protective or risk factors (Courtet, 2016; Demotes-Mainard et al., 2006; Gibbons and Mann, 2011). Indeed, the protective effects of lithium to limit suicidal behaviour in patients suffering from mood disorders and clozapine in schizophrenia patients have been suggested for many years (Cipriani et al., 2013; Hennen and Baldessarini, 2005). Nevertheless, an increase in suicidal risk has been associated with several drugs, such as antidepressants, anticonvulsants, and medications used for smoking cessation (Fergusson et al., 2005; Moore et al., 2011; Patorno et al., 2010). For example, in a large European study with 3390 manic or mixed patients with bipolar disorder, the introduction of anticonvulsants was associated with an increased risk of SA (Bellivier et al., 2017). However, while studies faced different clinical contexts and limitations (e.g., confounding by indication bias), some associations were no longer found in larger pharmacoepidemiological studies. Moreover, the same psychotropic treatment might be a protective factor or a risk factor depending on the patient's clinical features, such as age. For instance, antidepressants lead to an increased risk of deliberate self-harm for patients under 24 years of age and a decreased risk for adults older than 24 years (Miller et al., 2014).

It has also been suggested that an adequate psychotropic drug prescription for a mental illness may decrease the risk of suicide (Gianatsi et al., 2020; Oquendo et al., 1999). For

example, while depression is a common risk factor for suicidal behaviour, treatment with antidepressants may reduce the risk of suicide (Hawton et al., 2013; Zalsman et al., 2016). However, among patients suffering from major depressive disorder, only 21.2% are treated with an antidepressant, and 18.4% are treated with only anxiolytics (Bryson et al., 2004). The same findings were observed in subjects suffering from schizophrenia for whom treatment with antipsychotics reduced the risk of death by suicide (Lester, 2009). In contrast, among subjects who died by suicide, 24% had not received any treatment even though a psychiatric diagnosis had been established (Gianatsi et al., 2020).

To our knowledge, patients with a history of previous SA present a higher risk of suicide reattempt (Christiansen et al., 2007; Large et al., 2011; Vuagnat et al., 2019), and the role of psychotropic drugs in the risk of suicide reattempt is unclear. While psychiatric disorders increase the risk of suicidal behaviour, the use of appropriate prescriptions in accordance with the patient's mental disorder seems to be crucial for preventing suicide among these high-risk patients (Fazel et al., 2019).

The objective of the present study was to determine, among subjects who attempted suicide, psychotropic drug exposures up to 14 months after an SA and to evaluate the association between the risk of suicide reattempt within 6 and 14 months after a SA with the use since inclusion up to 6 or 14 months of medications from different classes of psychotropic drugs, combination pairs and treatment adequacy.

# METHOD

## Study Design

A prospective observational cohort of 972 subjects from the ALGOS study was used for the analysis. The ALGOS study is a multicentric, prospective, single-blind, randomized and controlled clinical trial with two parallel groups. Participants in the intervention group received a brief contact intervention for 6 months (Vaiva et al., 2011), and control participants did not receive any intervention. Participants from both groups were used in the present study. This study was conducted in 23 French emergency departments. Patients included were men and women of legal age with a SA in the 7 days prior to inclusion, regardless of the method used for the SA. Patients with no suicidal intent, those who were homeless, those who were under guardianship, or patients with more than 4 SAs in the past 3 years were excluded from the study. Multirepeaters were excluded from this trial, as brief contact interventions have been demonstrated to be less effective for these subjects (Vaiva et al., 2006). All participants in the ALGOS study provided signed consent.

This study received authorization from AFFSAPS (number NCT01123174) and was approved by the Committee for the Protection of Persons in the North-West Region (CPP North-West decision 09/63). The ALGOS study was registered at ClinicalTrials.gov (NCT01123174).

## Collected data

At inclusion, sociodemographic characteristics (age, sex, family and work status), the number of previous SAs, the method of SA (all methods, including drug overdose and acute alcohol use) and a questionnaire based on Beck's intentionality scale were collected for all subjects (Beck et al., 1972). Psychotropic drug prescriptions were not assessed at inclusion.

At 6 and 14 months, the psychotropic drugs taken by the patients since inclusion (antidepressants, benzodiazepines, hypnotics, hydroxyzine, sedative antipsychotics, other antipsychotics, lithium, anticonvulsants, analgesics, opioid maintenance therapy and maintenance treatment for alcohol dependence), the psychiatric diagnosis using the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998), the number of suicide reattempts and the date of the first reattempts were assessed for all participants through a standardized telephone interview.

## Primary and secondary outcomes

The primary outcome was suicide reattempt within 6 months. The secondary outcome was suicide reattempt within 14 months. At 6 and 14 months, the number of suicide reattempts

and the date of the first reattempt were ascertained for all participants through a standardized telephone interview by trained psychologists from the University Hospital of Lille.

Drug exposures

Prescriptions were classified according to the Anatomical Therapeutic Chemical (ATC) classification (World Health Organization, n.d.). Exposures to different psychotropic drugs since inclusion were evaluated during the telephone interview: antidepressants, benzodiazepine anxiolytics, hypnotics, hydroxyzine, sedative antipsychotics (levomepromazine, cyamemazine and loxapine), other antipsychotics, lithium, all anticonvulsants (except benzodiazepine derivates), analgesics (general analgesics and opioids), opioid maintenance therapy and maintenance treatment for alcohol dependence. For the purpose of the study, zopiclone, zolpidem and alimemazine were classified as hypnotics. The most frequently combined pairs of medications were used in the statistical analysis. A combination pair was determined to be frequent when more than 5% of the participants were exposed to it within 6 or 14 months. Thus, the combination pairs of concurrent use of antidepressants and benzodiazepines, antidepressants and hydroxyzine, antidepressants and hypnotics, benzodiazepines and hypnotics, and benzodiazepines and analgesics were used in the statistical analysis.

A drug prescription was found to be adequate when it was prescribed for the appropriate mental illness according to the current international guidelines (e.g., antidepressants prescribed for patients suffering from major depressive disorder, atypical antipsychotics or anticonvulsants or lithium for bipolar disorder).

Statistical analysis

Descriptive analysis

Descriptive statistics were calculated for sociodemographic characteristics, psychiatric diagnoses, psychotropic drug classes consumed and treatment combinations. Continuous variables are presented as the means and standard deviations (SD). The 95% confidence intervals (95% CIs) were calculated using the central limit theorem. Discrete variables are expressed as frequencies and percentages. Finally, for patients whose status regarding suicide reattempt and drug consumption were known, the Kaplan-Meier estimate enabled us to draw survival curves and to estimate SA-free survival. Curves were stratified according to psychotropic drug consumption.

Analysis of primary and secondary outcomes

First, missing data were imputed using the multiple imputation method by chained equations, assuming the data were missing at random. The covariates used to generate the multiple imputed data sets were all the data collected at inclusion, 6 and 14 months. Fifty imputed datasets were generated and combined according to Rubin's rules using the MICE package of R software (Van Buuren and Groothuis-oudshoorn, 2011). After imputation for missing data, the relationship between the different drug classes, psychiatric diagnosis, randomization group, sociodemographic factors, and suicide reattempt within 6 months was assessed using a bivariate Cox model. Then, variables with a p value $< 0.2$ in the previous analysis were studied using a multivariable Cox model with descendant stepwise variable selection, and p values $< 0.05$ were considered significant. The secondary outcomes were evaluated with the same method. R software version 3.6.1 was used for all analyses.

Sensitivity analysis

Logistic regressions were also used in the sensitivity analysis in the same manner as the Cox model and with the same outcomes.

## RESULTS

*Patients at inclusion*

A total of 972 participants were included in the study (see **Table 1**). More than half were women (63.6%) and first-time attempters (53.3%), with an average age of 38 years old. The most common method of SA prior to inclusion was medication overdose (94%).

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*Insert table 1 about here.*

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*Psychotropic drug consumption*

Psychotropic drug prescriptions from the time of inclusion to 6 months later were evaluated for 670 patients (68.9%), and from inclusion to 14 months in 628 (64.6%). Half of the patients were prescribed antidepressants (48.1% within 6 months and 50.5% within 14 months) and anxiolytics (47.2% within 6 months and 48.4% within 14 months) (see **Table 2**). Approximately one-fifth of the patients had taken hypnotics (20.7% within 6 months and 25% within 14 months). Concomitant use of antidepressants and benzodiazepines was relatively frequent within 6 and 14 months after SA (28.4% and 30.9%, respectively), as was the concurrent use of antidepressants and hypnotics (14.2% within 6 months and 17.4% within 14 months) or benzodiazepines and hypnotics (14% within 6 months and 15.6% within 14 months).

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*Insert table 2 about here.*

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Of 880 participants (90.5%) re-contacted at 6 months after inclusion, 117 (13.3%) had reattempted suicide. At 14 months after inclusion, 173 (21.1%) had reattempted suicide. The most common psychiatric diagnoses were mood disorders (198 (29.2%) at 6 months and 152 (24.4%) at 14 months), anxiety disorders (193 (28.5%) at 6 months and 114 (18.2%) at 14 months) and alcohol use disorders (124 (18.3%) at 6 months and 103 (16.3%) at 14 months).

*Missing data*

The patient's status regarding suicide reattempt was missing for 9.5% of participants at 6 months and 15.8% at 14 months. Patients lost to follow-up within 14 months had almost the same distribution of socio-demographic characteristics as those who were not missing (29% less than 26 years old, 57% aged from 26 to 50 years, 14% above 50 years old, 60% women,

53% first-time attempters, 45.1% in couple, 64.4% employed, 91.6% SA by medication overdoses, 45.3% SAs with acute alcohol use). Data on psychotropic drug consumption were only available for 670 patients at 6 months and 628 patients at 14 months. Additionally, only 678 and 630 patients agreed to complete the MINI at 6 months and 14 months, respectively.

*Survival curve analysis*

The SA repeat-free survival curves within 14 months were stratified according to psychotropic drug consumption and are presented in **Figure 1**. Within 6 months after SA, survival probability was similar for the different psychotropic classes except for lithium, anticonvulsants and maintenance treatment for alcohol dependence. Treatment with lithium seemed to provide a higher survival probability, whereas anticonvulsants and maintenance treatment for alcohol dependence were association with lower survival probabilities. The lowest survival probability within 14 months after SA was found for the consumption of sedative antipsychotics, anticonvulsants and maintenance treatment for alcohol dependence.

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*Insert Figure 1 about here.*

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*Association between psychotropic classes and the risk of suicide reattempt within 6 months (primary outcome)*

None of the psychotropic drug classes or combination pairs were associated with suicide reattempt within 6 months after SA in the multivariable Cox model (see **Table 3**). However, a history of previous SA before the index SA (hazard ratio with 95% CI (HR)=1.63 [1.12; 2.37], p=0.01), mood disorders (HR=1.58 [1.12; 2.37], p=0.01) and anxiety disorders (HR= 1.96 [1.30; 2.96], p<0.01) were risk factors for suicide reattempt within 6 months.

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*Insert table 3 about here.*

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*Association between psychotropic classes and the risk of suicide reattempt within 14 months*

Within 14 months after SA, the use of benzodiazepines was statistically associated with suicide reattempt (HR=1.87 [1.25; 2.81], p<0.01), as was the use of hypnotics (HR=1.49 [1.03; 2.17], p=0.04), a history of more than 1 previous SA (HR=1.65 [1.22; 2.23], p<0.01) and

substance use disorder (HR=1.74 [1.20; 2.53], p<0.01) after adjustment for confounding variables.

*Concurrent use of classes and the risk of suicide reattempt within 6 and 14 months*

None of the combination pairs of psychotropic drug classes were associated with suicide reattempt within 6 months. Concomitant use of benzodiazepines and hypnotics was also associated with an increased risk of suicide reattempt within 14 months (HR=1.80 [1.17; 2.72], p=0.01).

*Adequacy between psychiatric diagnosis and psychotropic drug consumption*

Patients suffering from anxiety disorder and major depressive disorder appeared to benefit from appropriate drug prescriptions (73.3% and 65.3% at 6 months, respectively; 81.2% and 81.6% at 14 months, respectively), whereas half of patients suffering from bipolar disorder or psychotic disorder had inadequate treatment (55.6% and 50% at 6 months, respectively; 59.5% and 40% at 14 months) (see **Table 4**). Adequacy between mental disorders and psychotropic drug prescriptions was not significantly associated with the risk of suicide reattempt within 6 and 14 months.

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*Insert table 4 about here.*

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*Sensitivity analysis*

Logistic regressions were also used in sensitivity analysis with the same outcomes, and they conferred the same results.

# DISCUSSION

Here, we present a pharmacoepidemiological study exploring the risk of suicide reattempts associated with the use of psychotropic drugs in patients who have already attempted suicide. While our main results did not show an association between psychotropic drug use and suicide reattempt after 6 months of follow-up, we demonstrated that the use of benzodiazepines or hypnotics or a combination of both were associated with suicide reattempt within 14 months after a previous SA. We also found good treatment adequacy for patients with major depressive disorder and anxiety disorders and psychotropic drug consumption but poor adequacy for bipolar or psychotic disorders. However, treatment adequacy did not seem to be associated with suicide reattempt at 6 or 14 months.

We found that the use of benzodiazepines was associated with a higher risk of suicide reattempt within 14 months after an SA, with an almost twofold increase in the risk of reattempt (HR=1.87 [1.25; 2.81], p<0.01). Notably, benzodiazepines were not associated with a higher risk of suicide reattempt within 6 months. This could be explained by a lower protective effect of the drug over time or by a cumulative risk effect that grows with treatment duration. This result seems to be important given the widespread prescription of benzodiazepines in France (Benard et al., 2017). A recent review of placebo-controlled trials and case-control studies in a variety of populations also found that benzodiazepine use is associated with an increased risk of SA or death by suicide (Dodds, 2017). The authors of this review hypothesized that benzodiazepine consumption increases aggression and impulsivity by mediating GABAA receptors or that discontinuation or reduction in dosage may be responsible for withdrawal or rebound in symptoms. Nevertheless, in 2002, a study found there was no longer an association between benzodiazepine use and SA after adjustment for borderline personality disorder (Lekka et al., 2002).

According to our results, hypnotic use also appears to be a risk factor for suicide reattempt within 14 months after an SA (HR=1.49 [1.03; 2.17], p=0.04). A review of the scientific literature indicated that most studies found similar associations between the use of hypnotics and the risk of suicide (Wang et al., 2016). More specifically, a recent epidemiological study found an elevated risk of suicide with zolpidem use after 80 months of observation (HR=2.01 [1.58; 2.56], p < 0.001). However, the main limitation of these studies was that none adjusted the analyses for possible confounding factors such as depression or sleep disorders. While our analysis was adjusted for mood disorders, the association of sleep disorders with suicidal behaviour has also been demonstrated and was not assessed in our study (Malik et al., 2014; Pigeon et al., 2012). The analysis of the National Comorbidity Survey

Replication also noted that hypnotic use in the past year was significantly associated with SA (adjusted OR = 3.4; $p < 0.01$) after adjustment for sleep disturbances and was a stronger predictor than insomnia for SA (Brower et al., 2011). The causal effect of hypnotic medication on suicidal behaviour is not clear. It has been suggested that hypnotics may cause parasomnias or an impairment of judgement and promotion of violent and risky behaviours that may lead to suicidal ideations (McCall et al., 2017).

The analysis of drug class combinations taken during the 14 months following inclusion showed an almost two-fold higher risk of SA with concomitant use of benzodiazepines and hypnotics (HR=1.80 [1.17; 2.72], p=0.01). The study of the relationship between drug class combinations and the risk of SA seems to have rarely been explored in the current scientific literature. A Korean case-control study based on the National Health Insurance Service found a 2.80-fold higher risk of suicide among patients taking benzodiazepines and antidepressants with zolpidem in comparison to those taking zolpidem alone (adjusted OR= 2.80 [1.38; 5.70]) (Sung et al., 2019). Regarding elderly individuals, a Swedish case-control study found a four-fold increased risk of suicide among seniors who used sedative or hypnotic treatments after adjusting for psychiatric diagnosis (Carlsten, 2009).

Interestingly, different studies have assessed the association between consumption of the different classes of psychotropic drugs and the risk of suicidal behaviour in other specific populations. Among schizophrenia patients, the use of benzodiazepine was also associated with an increased risk of death by suicide (HR=3.83 [1.45; 10.12]) (Tiihonen et al., 2012). In elderly individuals, the same results were found in a population-based study, with an association between benzodiazepine use and elevated suicide risk (Voaklander et al., 2008).

Surprisingly, no psychotropic drug was associated with a lower risk of suicide re-attempt in our study, though it has been demonstrated that lithium and clozapine (in schizophrenia patients) are associated with a lower risk of suicide reattempt (Cipriani et al., 2013; Taipale et al., 2020). These results were not replicated in our study, probably because of the low number of included patients taking clozapine or benefitting from lithium prescriptions.

Almost 70% of the subjects in our study were prescribed psychotropic drugs, most of which were antidepressants or anxiolytics. This result is consistent with the international literature. In fact, antidepressant prescriptions were given to 42.8% of patients who presented to the emergency department with suicidal ideation, behaviour or self-injury in Canada and 97.2% of subjects who attempted suicide in Spain (Irigoyen et al., 2019; Katz et al., 2018).

In our study, half of the patients did not receive adequate medication treatment according to their psychiatric diagnosis. This “treatment gap” could be involved in suicide risk (Mann et al., 2005; Oquendo et al., 2002). Interestingly, our results are consistent with the national and international literature, as it has been shown that in France, Brazil and the USA, most subjects suffering from a psychiatric disorder did not receive adequate treatment or seek mental health services (Font et al., 2018; Moreno-Küstner et al., 2011; Moreno and Andrade, 2005; Oquendo et al., 2002).

Strengths and limitations

One of the strengths of this study is the relatively high number of participants included, with a distribution of sociodemographic and clinical characteristics that are typically found in a natural cohort of individuals who attempted suicide. Studies on psychotropic drugs and suicide are challenged by confounding by indication bias, whereby suicidal patients are prescribed psychotropic medications because they are seeking treatment due to increased distress. To counter this bias, the analysis was adjusted for psychiatric diagnosis to improve the interpretation of the results. For instance, we did not find any association between maintenance treatment for alcohol dependence and suicide risk after adjustment for substance use disorder, which is a main risk factor for suicidal behaviour (Yuodelis-Flores and Ries, 2015).

This study also has some limitations. First, there was a large amount of missing data, sometimes as much as 35% of the data depending on the variable studied. Nevertheless, this bias was reduced by using multiple imputation for missing data, generating 50 imputed tables that were combined for the analyses. This robust imputation method is limited, as it assumes that data are missing at random, but patients lost to follow-up may have specific psychiatric features. However, those subjects had the same distribution of socio-demographic characteristics as those who were not lost to follow-up. Second, the retrospective information collection during telephone interviews at 6 and 14 months after inclusion was self-reported, could not be verified and was exposed to the risk of loss of information. Then, we a priori set the alpha threshold at 0.05 despite multiple tests. Indeed, only one multivariate model was used for primary outcome assessment, and secondary outcomes were exploratory results and cannot be assumed to demonstrate a causal link. Moreover, psychotropic drug prescriptions were not assessed at inclusion but only at 6 and 14 months later. This information bias did not allow us to know if psychotropic drugs were used before or after suicide reattempt. This design also did not permit us to evaluate the effect of treatment initiations on suicide re-attempts. In addition, the study design did not permit us to assess whether psychotropic drugs were used

concomitantly or one after another over the period. Third, subjects were included in emergency settings if they agreed to participate in the ALGOS trial. This inclusion criteria creates potential for selection bias. Finally, this study analysed classes of psychotropic drugs, but the study design does not permit an assessment of more specific effects of certain subclasses or drugs such as lithium (too few patients benefited from it) or the effect according to the daily dose prescribed.

Perspectives

The objective of the ALGOS study was to assess a post-hospital monitoring device for suicidal patients by following the ALGOS algorithm. The analysis of the drug consumption of participants during the telephone interviews brought a new dimension to this study through a pharmacoepidemiological approach. Evaluation of drug prescriptions on a larger scale in national registries could allow for more specific analyses of certain subclasses of psychotropic drugs or certain medications. In addition, sleep disorders, impulsivity dysregulation and borderline personality disorders are widespread in the psychiatric population and in suicidal patients. Their consideration in a future study would allow for better adjustment of these confounding factors and more specific analyses of the pharmacological effect of drug classes.

# CONCLUSION

This study investigated psychotropic drug prescriptions and the association between the prescription of certain classes and a higher risk of suicide reattempt within 14 months. Benzodiazepine and hypnotic prescriptions were found to be associated with a higher risk of suicide reattempt within 14 months. The early identification of a positive association between psychotropic drugs and risk of suicidal behaviour is important for the prevention of suicide reattempts. Special precautions should be considered when prescribing psychotropic drugs for individuals with a previous SA, who are at elevated risk of suicide reattempt (Fazel and Runeson, 2020), such as prescribing with greater vigilance and prescribing appropriate treatments based on the psychiatric diagnosis. A more personalized pharmacological approach to patients who have attempted suicide is necessary to prevent suicide reattempts or deaths by suicide.

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*Table 1. Baseline Characteristics of Participants.*

| Characteristics | All Patients (N = 972) |
|---|---|
| **Intervention group** | |
| **ALGOS** | 480 (49.4) |
| **Control** | 492 (50.6) |
| **Age, mean ± SD** | 38 ± 13.3 |
| **18–26 y** | 226 (23.3) |
| **26–50 y** | 558 (57.4) |
| **> 50 y** | 188 (19.3) |
| **Sex** | |
| **Men** | 354 (36.4) |
| **Women** | 618 (63.6) |
| **Marital status** | |
| **Single** | 515 (53.1) |
| **In couple** | 455 (46.9) |
| **Working status** | |
| **Employed** | 619 (63.9) |
| **Unemployed** | 349 (36.1) |
| **First attempt** | 518 (53.3) |
| **Suicide attempt by medication overdose** | 912 (94) |
| **Suicide attempt with acute alcohol use** | 417 (43.7) |

***Table 2. Psychotropic drug classes and combination pairs used since inclusion evaluated at 6 and 14 months.*** *(*1 number of patients having at least this treatment, irrespective of other treatments; 2 number of patients having at least this pair of treatments, irrespective of other treatments)

| Psychotropic drugs | 6 months (N= 670) | 14 months (N= 628) |
|---|---|---|
| **Antidepressants**[1] | 322 (48.1) | 317 (50.5) |
| **Anxiolytics**[1] | 316 (47.2) | 304 (48.4) |
| **Benzodiazepines**[1] | 267 (39.9) | 263 (41.9) |
| **Hydroxyzine**[1] | 45 (6.7) | 46 (7.3) |
| **Sedative antipsychotics**[1] | 26 (3.9) | 35 (5.6) |
| **Hypnotics**[1] | 139 (20.7) | 157 (25.0) |
| **Analgesics**[1] | 58 (8.7) | 66 (10.5) |
| **Anticonvulsants**[1] | 42 (6.3) | 35 (5.6) |
| **Antipsychotics (others)** [1] | 30 (4.5) | 33 (5.3) |
| **Lithium**[1] | 5 (0.7) | 10 (1.6) |
| **Maintenance treatment of alcohol dependence**[1] | 25 (3.7) | 27 (4.3) |
| **Opioid maintenance therapy**[1] | 2 (0.3) | 3 (0.5) |
| **At least one psychotropic drug** | 451 (67.4) | 442 (70.4) |
| **Combination pair** | | |
| **Antidepressant - Benzodiazepine**[2] | 190 (28.4) | 194 (30.9) |
| **Antidepressant - Hydroxyzine**[2] | 31 (4.6) | 32 (5.1) |
| **Antidepressant - Hypnotic**[2] | 95 (14.2) | 109 (17.4) |
| **Benzodiazepine – Hypnotic**[2] | 94 (14.0) | 98 (15.6) |
| **Benzodiazepine – Analgesics**[2] | 23 (3.4) | 33 (5.3) |

***Figure 1. SA-repeat-free survival within 14 months, stratified by psychotropic drugs.*** *(Figure A: Survival curve according to antidepressant, anxiolytic (benzodiazepine, hydroxyzine and sedative antipsychotic) and hypnotic consumption. Figure B: Survival curves according to other antipsychotics, lithium, anticonvulsants, analgesics and maintenance treatment for alcohol dependence)*

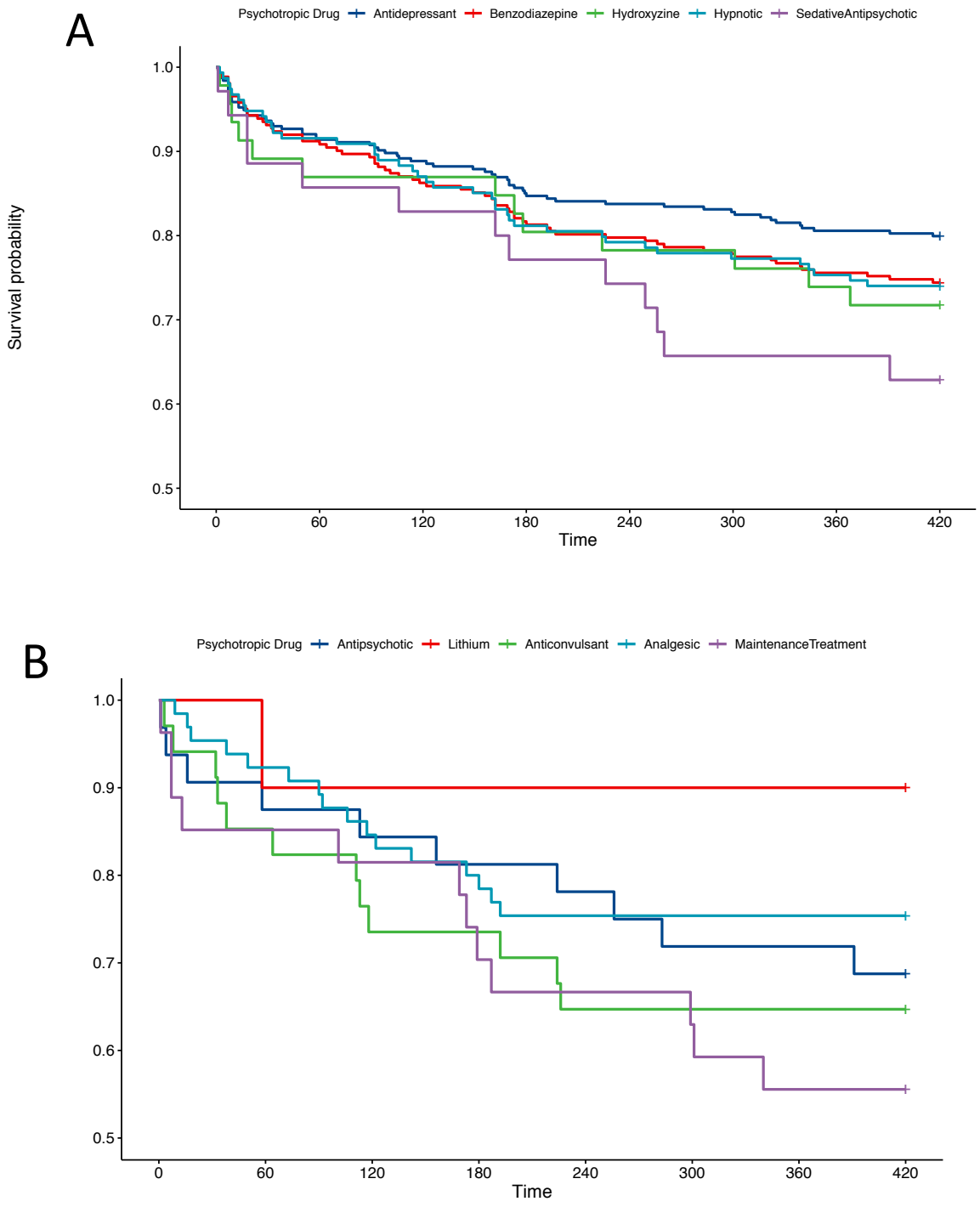


***Table 3. Association between classes of psychotropic drugs and SA reattempt within 6 and 14 months.***

| Factor | 6 months | | | | 14 months | | | |
|---|---|---|---|---|---|---|---|---|
| | HR (95CI)* | p* | adjusted HR (95CI)** | p** | HR (95CI)* | p* | adjusted HR (95CI)** | p** |
| **Randomization group (ref.=ALGOS)** | | | | | | | | |
| **Control** | 1.34 [0.94;1.92] | 0.10 | | | 1.27 [0.94;1.70] | 0.12 | | |
| **Sex (ref.=male)** | | | | | | | | |
| **Female** | 0.82 [0.57;1.18] | 0.29 | | | 0.88 [0.65;1.18] | 0.39 | | |
| **Age (ref.= 18-26)** | | | | | | | | |
| **26-50** | 1.85 [1.09;3.13] | 0.02 | | | 1.66 [1.07;2.57] | 0.02 | | |
| **> 50** | 1.72 [0.94;3.17] | 0.08 | | | 1.53 [0.92;2.54] | 0.10 | | |
| **Non-First-time attempter** | 1.79 [1.23;2.59] | <0.01 | 1.63 [1.12;2.37] | 0.01 | 1.83 [1.36;2.47] | <0.01 | 1.65 [1.22;2.23] | <0.01 |
| **Marital status (ref.= single)** | | | | | | | | |
| **In couple** | 0.79 [0.55;1.15] | 0.22 | | | 0.78 [0.58;1.06] | 0.11 | | |
| **Working status (ref.= employed)** | | | | | | | | |
| **Unemployed** | 1.31 [0.92;1.88] | 0.14 | | | 1.31 [0.97;1.76] | 0.07 | | |
| **Psychiatric diagnosis** | | | | | | | | |
| **Mood disorder** | 2.18 [1.47;3.24] | <0.01 | 1.58 [1.12;2.37] | 0.01 | 1.72 [1.25;2.38] | <0.01 | | |
| **Anxiety disorder** | 1.50 [1.03;2.18] | 0.04 | | | 1.95 [1.41;2.70] | <0.01 | | |
| **Psychotic disorder** | 1.27 [0.8;2.02] | 0.30 | | | 1.88 [1.33;2.65] | <0.01 | | |
| **Substance use disorder** | 2.42 [1.67;3.52] | <0.01 | 1.96 [1.30;2.96] | <0.01 | 2.38 [1.73;3.29] | <0.01 | 1.74 [1.20;2.53] | <0.01 |
| **Eating disorder** | 1.13 [0.72;1.77] | 0.59 | | | 1.70 [1.21;2.40] | <0.01 | | |
| **Psychotropic drug** | | | | | | | | |
| **Antidepressant** | 1.69 [1.09;2.61] | 0.02 | | | 1.44 [1.01;2.06] | 0.05 | | |
| **Benzodiazepines** | 1.86 [1.19;2.89] | 0.01 | | | 2.48 [1.67;3.67] | *<0.01* | 1.87 [1.25;2.81] | <0.01 |
| **Sedative antipsychotics** | 1.47 [0.96;2.26] | 0.07 | | | 2.07 [1.47;2.94] | *<0.01* | | |
| **Hydroxyzine** | 1.53 [1.05;2.23] | 0.03 | | | 1.81 [1.24;2.63] | *<0.01* | | |
| **Hypnotics** | 1.47 [0.99;2.18] | 0.06 | | | 2.26 [1.64;3.13] | <0.01 | 1.49 [1.03;2.17] | 0.04 |
| **Other antipsychotics** | 1.44 [0.96;2.15] | 0.08 | | | 1.96 [1.40;2.74] | <0.01 | | |
| **Lithium** | 1.37 [0.88;2.14] | 0.16 | | | 1.74 [1.23;2.45] | <0.01 | | |
| **Anticonvulsants** | 1.52 [1.04-2.21] | 0.03 | | | 2.19 [1.61;2.98] | <0.01 | | |
| **Analgesics** | 1.37 [0.94;2.01] | 0.10 | | | 1.90 [1.38;2.62] | <0.01 | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Maintenance treatment of alcohol dependence** | 1.62 [1.05;2.50] | 0.03 | | | 2.08 [1.47;2.94] | <0.01 | | |
| **Combination pair** | | | | | | | | |
| **Antidepressant and Hypnotic** | 1.38 [0.92;2.07] | 0.12 | | | 2.06 [1.46;2.91] | <0.01 | | |
| **Antidepressant and Benzodiazepine** | 1.48 [0.97;2.26] | 0.07 | | | 2.10 [1.42;3.10] | <0.01 | | |
| **Antidepressant and Hydroxyzine** | | | | | 1.77 [1.23;2.53] | <0.01 | | |
| **Benzodiazepine and Hypnotic** | 1.57 [1.03;2.38] | 0.04 | | | 2.42 [1.69;3.46] | <0.01 | 1.80 [1.17;2.72] | 0.01 |
| **Benzodiazepine and Analgesic** | | | | | 2.02 [1.43;2.85] | <0.01 | | |

** Hazard ratio and p-value estimated by bivariate Cox model*

*** Adjusted hazard ratio and p-value estimated by multivariate Cox model*

*p = p value*

***Table 4. Association between treatment adequacy and SA reattempt within 6 and 14 months.***

| Psychiatric disorder | 6 months | | | 14 months | | |
|---|---|---|---|---|---|---|
| | n/N (%) | HR (95CI)* | p* | n/N (%) | HR (95CI)* | p* |
| **Major depressive disorder** | 66/101 (65.3) | 1.14 [0.58;2.28] | 0.70 | 40/49 (81.6) | 0.92 [0.48;1.78] | 0.80 |
| **Anxiety disorder** | 142/193 (73.6) | 1.37 [0.59;3.21] | 0.46 | 91/112 (81.2) | 1.27 [0.55;2.93] | 0.56 |
| **Bipolar disorder** | 20/36 (55.6) | 0.94 [0.45;1.97] | 0.88 | 25/42 (59.5) | 0.94 [0.43;2.04] | 0.87 |
| **Psychotic disorder** | 2/4 (50.0) | 1.21 [0.62;2.38] | 0.58 | 2/5 (40.0) | 1.09 [0.54;2.21] | 0.81 |
| **Alcohol use disorder** | 23/124 (18.5) | 1.08 [0.40;2.93] | 0.88 | 15/103 (14.6) | 1.28 [0.68;2.41] | 0.44 |
| **TOTAL** | 253/458 (55.2) | | | 173/311 (55.6) | | |

** Hazard ratio and p-value estimated by bivariate Cox model*

*p = p value*

# II. ANALYSE DE LA MORTALITE APRES UNE TS

Nous évoquions dans l'introduction que l'espérance de vie était fortement réduite chez les suicidants. Récemment, une étude avait estimé que l'espérance de vie était réduite de 8 à 18 ans après une première TS selon le sexe et l'âge de survenue (24). Néanmoins, les causes de décès prématuré après une TS ont été peu étudiés dans la littérature scientifique. En effet, de nombreuses études se sont intéressées aux causes de décès après n'importe quel passage à l'acte auto-agressif. Par ailleurs, on peut s'attendre à des taux de décès par suicide particulièrement élevés. Or, les dernières méta-analyses ont également estimé le taux de décès par suicide après un passage à l'acte auto-agressif (79,80). Dans ce chapitre, nous verrons plus précisément le devenir des patients ayant fait une TS en estimant le risque de décès par suicide dans les années suivant la TS et en déterminant les causes de décès et les facteurs de risque qui y sont associés.

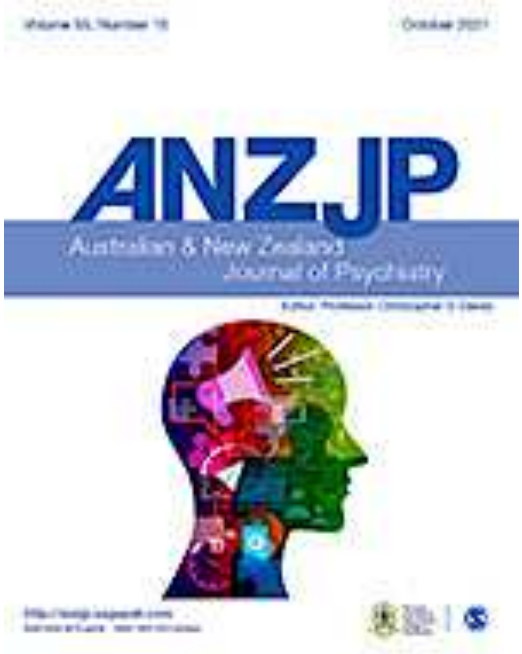
## 1. Estimation du taux de décès par suicide après une TS

Nous nous sommes intéressés en premier lieu aux causes psychiatriques de surmortalité chez les suicidants et notamment le décès par suicide. Plusieurs études ont tenté d'estimer le taux de décès par suicide chez les suicidants et retrouvaient un taux allant de 1,4% à 4 ,4% selon la sous-population spécifique qui était étudiée. De plus, dans de précédentes méta-analyses, le taux de décès par suicide après un passage à l'acte était estimé à 1,6% à 1 an et 3,9% à 5 ans (80). Cependant, même si la définition des passages à l'acte auto-agressifs inclut les TS et qu'ils partagent des facteurs de risque, le risque de décès par suicide après une TS est probablement différent. L'objectif de notre étude était d'estimer le taux de décès par suicide à 1, 5 et 10 ans après une TS à l'aide d'une revue de la littérature et d'une méta-analyse.

Les essais cliniques randomisés et les études de cohorte publiées entre 1970 et 2020 ont été inclus dans notre revue de littérature. Les taux de décès par suicide à 1, 5 et 10 ans après une TS ont été estimés dans une méta-analyse. Les études étaient inclues quel que soit le lieu d'inclusion des patients, la classe d'âge étudiée et la pathologie psychiatrique. Notre méta-analyse comprenait ainsi 41 articles publiés dans des revues internationales. Le taux de décès par suicide après une TS était estimé à 2,8% à 1 an, 5,6% à 5 ans et 7,4% à 10 ans. Estimer ainsi les taux de décès par suicide et déterminer ainsi les périodes les plus à risque de suicide est crucial si l'on souhaite améliorer la prévention du suicide.

### Article 3. Mortalité par suicide après une TS non fatale : une revue de la littérature et méta-analyse

Ce troisième article a été publié dans l'Autralian & New Zealand Journal of Psychiatry en juin 2022.




# Suicide mortality after a nonfatal suicide attempt: A systematic review and meta-analysis

Alice Demesmaeker[1,2], Emmanuel Chazard[3], Aline Hoang[1], Guillaume Vaiva[1,2,4] and Ali Amad[1,2]

# Suicide mortality after a nonfatal suicide attempt. A systematic review and meta-analysis.

Alice DEMESMAEKER1* (MD, MSC), Emmanuel CHAZARD2 (MD, PhD), Aline HOANG1 (MD), Guillaume VAIVA1,3 (MD, PhD), Ali AMAD1 (MD, PhD)

1) Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, F-59000 Lille, France

2) Univ. Lille, CHU Lille, ULR 2694 Metrics, CERIM, Public Health Dept., F-59000 Lille, France

3) Centre National de Ressources et de Résilience (CN2R), F-59000 Lille, France

*Corresponding Author

Dr Alice DEMESMAEKER (MD, PhD)

Hôpital Fontan, CHU de Lille, F-59037, Lille cedex, France

Email: alice.demesmaeker@chu-lille.fr

Tel: + 33 3 20 44 42 15 Fax: +33 3 20 44 62 65

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## ABSTRACT

INTRODUCTION: Deliberate self-harm (DSH) and suicide attempts (SAs) share common risk factors but are associated with different epidemiological features. While the rate of suicide after DSH has been evaluated in meta-analyses, the specific rate of death by suicide after a previous SA has never been assessed. The aim of our study was to estimate the incidence of death by suicide after a nonfatal SA.

METHOD: We developed and followed a standard meta-analysis protocol (systematic review registration—PROSPERO 2021: CRD42021221111). Randomized controlled trials and cohort studies published between 1970 and 2020 focusing on the rate of suicide after SA were identified in PubMed, PsycInfo and Scopus and qualitatively described. The rates of deaths by suicide at 1, 5 and 10 years after a nonfatal SA were pooled in a meta-analysis using a random-effects model. Subgroup analysis and meta-regressions were also performed.

RESULTS: Our meta-analysis is based on 41 studies. The suicide rate after a nonfatal SA was 2.8% (2.2-3.5) at one year, 5.6% (3.9-7.9) at five years and 7.4% (5.2-10.4) at ten years. Estimates of the suicide rate vary widely depending on the psychiatric diagnosis, the method used for the SA, the type of study, and the age group considered.

CONCLUSION: The evidence of a high rate of suicide deaths in the year following nonfatal SAs should prompt prevention systems to be particularly vigilant during this period.



Keywords: suicide attempt, suicide, mortality, epidemiology.

## KEY POINTS

- The incidence of death by suicide after a nonfatal suicide attempt has never been assessed through a meta-analysis.
- Our meta-analysis based on 41 studies found a suicide rate after a nonfatal SA at 2.8% (2.2-3.5) at one year, 5.6% (3.9-7.9) at five years and 7.4% (5.2-10.4) at ten years.
- The evidence of a high rate of suicide deaths in the year following nonfatal SAs should prompt prevention systems to be particularly vigilant during this period.

## INTRODUCTION

Suicide is a leading cause of avoidable death worldwide, with approximately 800,000 deaths per year (World Health Organization, 2014). Suicide rates have been declining annually throughout the world since 2000 (Fazel and Runeson, 2020). Moreover, with at least 16 million per year, suicide attempts (SAs) are estimated to be 25 to 50 times more common than deaths by suicide (Fazel and Runeson, 2020). For several decades, many efforts have been made to highlight the risk factors involved in suicidal risk to reduce suicidal behavior, to protect those exposed to it and to implement suicide prevention programs (Demesmaeker et al., 2021; Hill et al., 2020; Zalsman et al., 2016).

In this context, deliberate self-harm (DSH), including SAs, has been particularly investigated, as they are more frequent, as the data on DSH are routinely collected at admission to hospital. Moreover, DSH are supposed to share risk factors for death by suicide (Knipe et al., 2019; Runeson et al., 2016). DSH is defined as an act of intentional injury or damage to the body, including nonfatal SA and all other injuries (e.g., self-poisoning, cutting or burning), irrespective of the suicidal intent to die or not (NHS Inform, n.d.). Moreover, DSHs have been the subject of more research because they do not require the researcher to establish the suicidal intent of the act (Huang et al., 2017; Wilkinson et al., 2011).

The scientific literature has already focused on the risk of death by suicide after a nonfatal DSH episode and the risk of suicides after discharge from nonpsychiatric settings through three literature reviews and meta-analyses (Carroll et al., 2014; Owens et al., 2002b; Wang et al., 2019). First, in 2002, a systematic review estimated the suicide rate after a nonfatal DSH episode at 1.8% at one year, 3.4% between 4 and 9 years and 6.7% over 9 years (Owens et al., 2002b). A more recent meta-analysis, in 2014, estimated the risk of suicide after hospital discharge for DSH to be 1.6% within the first year and 3.9% within 5 years (Carroll et al., 2014). Third, a meta-analysis on participants who presented with suicidal thoughts and

behaviors in nonpsychiatric settings found that the pooled suicide rate was 483 suicide deaths per 100,000 person-years (Wang et al., 2019). The first two studies cited above included all studies exploring DSH episodes to determine whether the suicidal intent for the episode was investigated or not and even whether self-injury leading to healthcare contact was a habitual nonsuicidal behavior (Carroll et al., 2014; Owens et al., 2002a). The latest review explored suicidal thoughts and behaviors after discharge from nonpsychiatric settings and therefore excluded a large number of subjects consulting for suicidal acts.

Interestingly, while the rate of suicide after a nonfatal DSH has been evaluated in systematic reviews and meta-analysis, the specific rate of death by suicide after an SA after discharge from psychiatric or nonpsychiatric healthcare services has never been assessed through a meta-analysis or other statistical analysis pooling multiple-source databases. Indeed, non-suicidal self-injury, generally covered by the term "self-harm", may be distinct from suicidal behavior; therefore, several authors have suggested establishing the suicidal purpose of a DSH episode to appropriately classify attempts into suicidal or nonsuicidal (De Leo et al., 2006; Fazel and Runeson, 2020; Nock, 2010; Oquendo and Courtet, 2015). Some authors have also suggested distinguishing these two terms since they are associated with different epidemiological features, providing more consistency in nomenclature and improving research on suicide prevention programs (Fazel and Runeson, 2020; Oquendo and Courtet, 2015).

The aim of our study was to estimate the incidence of death by suicide after a nonfatal SA. Therefore, we performed a systematic review and meta-analysis of published aggregated data. We hypothesized that the rate of death by suicide after a previous non-fatal SA must be higher than that after any DSH episode.

## METHODS

We developed and followed a standard meta-analysis protocol (systematic review registration—PROSPERO 2021: CRD42021221111).

### Types of participants

We reviewed studies involving patients with a history of a previous SA. Definitions by Beck "a situation in which a person has performed an actually or seemingly life-threatening behavior with the intent of jeopardizing his life, or to give the appearance of such an intent, but which has not resulted in death" (Beck et al., 1972) and O'Caroll "a potentially self-injurious behavior with a nonfatal outcome, for which there is evidence that the person had the intent to kill him/herself, but failed, was rescued or thwarted, or changed one's mind" were used to define a nonfatal SA. A serious SA is defined as "an attempt that would have been fatal had it not been for the provision of rapid and effective emergency treatment". Inclusion criteria were a history of SAs or a history of DSH or self-poisoning if a suicidal intent of the episode was mentioned. We excluded studies including participants with a history of DSH, self-poisoning or any self-injury if no suicidal intent was evaluated or reported.

### Types of interventions

Studies were eligible if they followed participants for at least one year and if they focused on the rate of subsequent death by suicide after a nonfatal SA.

### Types of outcomes

We considered as a primary outcome the one-year rate of deaths by suicide after a nonfatal SA. Secondary outcomes were the rate of suicide at 5 and 10 years after SA.

### Types of studies

Our review was restricted to cohort studies and randomized controlled trials (RCTs), regardless of the inclusion location (consultation, liaison services, hospital presentation or admission). For RCTs, only information from the control arm was considered exempt from any effect of the treatment studied. Studies focusing on specific age groups or specific psychiatric disorders were also included.

### Search strategy

We searched PubMed, PsycInfo and Scopus to identify all English- or French-language papers published between 1970 and 2020 using the following term combinations: “suicide attempt*” AND “mortality”. Personal collection of the authors and then the reference sections of all included papers were also browsed to identify any additional relevant studies.

Study selection

The eligibility assessment was performed independently in a blind standardized manner by two reviewers (AD and AH). Disagreements were resolved by consensus or in consultation with a third reviewer (AA). We checked for multiple papers published with the same cohort of patients and avoided duplicates.

Assessment of methodological quality

All studies were assessed for methodological quality prior to inclusion in the review using an appropriate tool from the Joanna Brigs Institute (critical appraisal tools for prevalence studies and randomized controlled trials, which can be found in https://jbi.global/critical-appraisal-tools) for assessing the risk of bias. Each question was scored from 0 to 2 (0: no, 1: unclear, 2: yes).

Data collection

For the included studies, the following data were extracted: characteristics of the study (year, design, country), characteristics of the participants (number of patients, specific age group, specific clinical context), duration of follow-up and rate of suicide mortality.

Data analysis

Aggregated data were used. First, we performed a qualitative analysis describing each study, its design and the outcomes observed. A quantitative synthesis of all evidence available from the cohort studies and RCTs was then performed.

The incidence of death by suicide was calculated as the number of participants who died by suicide within a given time frame. The duration of follow-up can vary for participants in a study. If participants were recruited and followed up over different periods of time, the mean duration of follow-up was taken into consideration, and the estimated risk of death was investigated.

The rate of deaths by suicide at 1, 5 and 10 years after a nonfatal SA was calculated and pooled using a random-effects model, and the proportions were transformed into logits. All

estimates are reported with their 95% confidence intervals (95% CIs). Second, subgroup analyses were performed investigating the relationship between different types of studies (i.e. cohort studies or randomized controlled trials), continents, specific age groups, year of publication, the characteristics (e.g. first SA, serious SA) and methods used for the SAs and the assessment of psychiatric disorders, and the rate of suicide. Third, we evaluated potential moderators: year of publication, mean age of participants and the total number of participants at baseline through meta-regression analysis.

Statistical heterogeneity was visually inspected on the forest plots and evaluated with the I2 index, and the Q statistic. Studies introducing substantial heterogeneity (I2 > 50% and/or p value of the Q test > 0.10) were identified and described. Then, sensitivity analysis without these studies was performed. The existence of a small study effect, suggestive of possible publication bias, was investigated graphically using a funnel plot.

All analyses were performed using R and the Metafor package (Viechtbauer, 2010). The results are presented according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Page et al., 2021).

# RESULTS

## Studies included

A total of 2642 papers were screened, and 41 were included in the meta-analysis (25 for 1-year suicide rate estimation, 14 for 5-year suicide rate and 11 for 10-year suicide rate) (see Table 1 and Figure 1)

Insert Table 1 and Figure 1 about here.

## Study characteristics, risk of bias within studies and qualitative analysis

### Study characteristics

Among the studies included in the quantitative analysis, 38 (92.7%) were cohort studies, and three (7.3%) were randomized controlled trials. Among the studies, 32 (78%) were undertaken in Europe, 7 (17%) in North America, and 2 (4.9%) in Asia. In addition, two studies focused specifically on mood disorders (one study on primary severe depression or melancholia and one study on inpatients suffering from major affective disorders (unipolar or bipolar depression), anxiety disorders, schizoaffective disorder or adjustment disorders) or on specific age groups (four on adolescents and two on the elderly). Six studies (15%) took only a single method or characteristic of SA into consideration: four studies on self-poisoning and two of all serious SAs. Finally, two studies specifically included participants with a first SA.

### Description of the RCTs

Three RCTs were considered for the qualitative analysis evaluating interventions for the prevention of a suicide reattempt (Hvid et al., 2011; Morthorst et al., 2012; Vaiva G et al.,c2018). conducted an RCT involving 133 participants (64 in the control group) admitted to the emergency department and clinical departments after a SA in Norway. Patients with major psychiatric diagnoses (schizophrenia, bipolar disorder, severe/psychotic depression) were not included. Vaiva et al. (Vaiva G et al., 2018) conducted an RCT on 1040 patients (494 in the control group) recruited in French emergency departments. (Morthorst et al., 2012) included 234 participants (120 in the control group) admitted to the acute emergency department, intensive care unit, pediatric units, and psychiatric emergency rooms. They excluded patients diagnosed with schizophrenia spectrum disorders and patients living in institutions. For these RCTs, the risk of bias was high due to not blinding the participants and personnel (see supplementary materials, Table 2).

### Description of the cohort studies

Bias was heterogeneous from low to high for the cohort studies (see supplementary materials, Table 2). The sample size was less than 100 participants for 9 (22.5%) cohort studies (see Table 1). The participants were not described in detail for 7 (17.5%) studies and were included from different care settings (emergency departments, psychiatric departments, poisoning centers, etc.). Moreover, the definition of an SA was heterogeneous across studies and constituted a risk of bias. In several studies, the definition used to characterize an SA was not specified or was imprecise (De Leo et al., 2002; Han et al., 2016; Ojehagen et al., 1992). All details are available in Table 1 and supplementary material Table 1.

Incidence of suicide at 1 year after a SA

The pooled estimated incidence of death by suicide within one year after a nonfatal SA was 2.77% (2.22-3.46) (see Table 2 and Figure 2). Heterogeneity among the studies was high (I2=93.5% and Q test: $p<0.01$).

Subgroup analysis showed different suicide rates when the psychiatric diagnosis and the type of study were taken into consideration ($p<0.05$). Indeed, participants with a mood disorder had a higher estimated incidence of subsequent suicide after a SA (12.00% (7.69-18.24)) compared to participants included regardless of a psychiatric disorder. Higher suicide rates were also found in cohort studies (2.88% (2.30-3.62)) than in randomized controlled trials (1.50% (0.80-2.81)). Subgroup analysis of studies focusing on self-poisoning and on people with a first SA showed nonsignificantly lower suicide rates (1.89% (1.22-2.91) and 1.71% (0.92-3.18), respectively).

Finally, meta-regressions did not highlight any effect of the year of publication, mean age of the participants or the total number of participants at baseline on the one-year suicide rate ($p>0.05$) (see supplementary materials, Table 1).

Insert Table 2, Table 3 and Figure 2 about here.

Incidence of suicide at 5 years after a SA

The pooled estimate of the 5-year suicide rate after a SA was 5.57% (3.88-7.95) (see Table 2 and Figure 3). The studies showed significant heterogeneity (I2=94.7% and the heterogeneity chi-squared test: $p<0.001$)).

Subgroup analysis highlighted significantly different estimates of five-year suicide risk according to specific age groups. Studies evaluating adolescents had a significantly lower incidence of suicide death at five years (1.58% (0.75-3.31)).

Finally, univariate meta-regressions showed an effect of the mean age of the participants on the five-year suicide rate with an increase in the incidence of subsequent death with age (p=0.02) and the findings suggested that the mean age of the participants explained 48% of the between-study variance in the estimates.

Insert Figure 3 about here.

Incidence of suicide at 10 years after a SA

The pooled estimate of the 10-year suicide rate after a nonfatal SA was 7.39% (5.21-10.38) (cf. Table 2 and Figure 3). Important heterogeneity existed among the studies with I2=96.3% and the heterogeneity chi-square test (p<0.001).

In the subgroup analysis, different rates of deaths by suicide were found according to the method used for the SA or characteristic of SA (p<0.01). People with a first SA had a lower incidence of subsequent deaths by suicide (5.59% (4.25-7.32), whereas patients who used self-poisoning or who did a serious SA had a higher incidence of subsequent deaths (10.57% (8.79-12.67) and 10.42% (8.09-13.34), respectively).

Meta-regressions did not highlight any effect of the year of publication, mean age of the participants or the total number of participants at baseline on the ten-year suicide rate (p>0.05).

Sensitivity analysis

According to the forest plot, two studies focusing on mood disorders and a study on the elderly were introducing substantial heterogeneity when estimating the suicide incidence at one year after an SA (Brådvik, 2003; Nordström, Åsberg, et al., 1995). The one-year suicide rate estimate was 2.34% (1.85-2.95) after exclusion of these studies. Nonetheless, heterogeneity remained high (I2=93.8%). In addition, two studies with small sample sizes appeared to be outliers when estimating the five-year suicide rate (Johnsson Fridell et al., 1996; Nielsen et al., 1990). Sensitivity analysis without these studies showed a five-year incidence of 5.20% (3.45-7.77). Finally, no study seemed to be an outlier when estimating the ten-year suicide rate after an SA. Thus, sensitivity analysis was not performed for the estimates of the ten-year suicide rate.

Assessment of publication bias

The investigation of the funnel plots did not show any evidence of publication bias.

Insert Supplementary Materials Figure 1 about here.

# DISCUSSION

Our literature review and meta-analysis based on 41 publications estimated the one-year suicide rate after a nonfatal SA at 2.8% (2.2-3.5), the five-year suicide rate at 5.6% (3.9-7.9) and the ten-year rate at 7.4% (5.2-10.4). Interestingly, the results of our subgroup analysis showed that the estimates of suicide rate varies widely depending on the psychiatric diagnosis, the method used for the SA, the type of study, and the age group considered. Moreover, our results suggested that the incidence of death by suicide was the highest during the first year after a nonfatal SA.

Notably, our study is the first meta-analysis to explore the rate of death by suicide after a nonfatal SA. Hence, two previous meta-analyses exploring the rate of suicide after any DSH episode found lower estimates (i.e., 1.6% (1.2-2.4) at one year and 3.9% (3.2-4.8) after 5 years) (Carroll et al., 2014; Owens et al., 2002b). Thus, the risk of subsequent death by suicide seems to be higher where there is suicidal intent. They also noticed a higher risk of death by suicide during the first year after a nonfatal SA. These results are of major importance in suicide prevention, as the key challenge is to determine which patients are at higher risk of death by suicide and when they are at highest risk.

In the subgroup analysis, a higher rate of deaths by suicide at one year was found for participants suffering from mood disorders compared to studies including participants regardless of the psychiatric diagnosis. These results are consistent with the scientific literature, as depression or bipolar disorder and a history of a previous SA are well-known risk factors for death by suicide (Arsenault-Lapierre et al., 2004; Chesney et al., 2014; Christiansen et al., 2007; Large et al., 2011). The interaction between these two factors may increase the risk of future death by suicide. Moreover, patients with major affective disorders and a history of previous SA were also associated with a higher risk of long-term suicide in a cohort of 954 participants (Fawcett et al., 1990).

Interestingly, our findings also indicated great variations in the rates of subsequent death by suicide in specific age groups in comparison to studies where all age groups were investigated. Concerning the adolescents, we found significantly lower suicide rates at five years after a SA. Therefore, the risk of death by suicide for adolescents appears to be high during the first year after a SA and then it seems to decrease. Nonetheless, the one-year rate was estimated according to a study on Swedish young men and may be affected by selection bias (Stenbacka and Jokinen, 2015). In a previous meta-analysis on suicide rates among people discharged from nonpsychiatric settings after presenting for suicidal behaviors, lower rates of future suicides were found for adolescents (Wang et al., 2019). Moreover, in long-term cohort

studies on adolescents, almost twice as many deaths occurred due to violent causes (i.e., substance abuse, road accident, drowning, homicide) rather than from suicide after a SA (Granboulan et al., 1995; Kotila and Lönnqvist, 1989).

In addition, we estimated nonsignificantly higher one-year suicide rates for the elderly according to two European studies (De Leo et al., 2002; Wiktorsson et al., 2011). Nonetheless, the sample sizes of these two studies were small, and wide confidence intervals were therefore estimated. The results of our meta-regression also noticed an association between age and death by suicide. Indeed, we found an increase in the incidence of death by suicide at five years with increasing age. Our results are consistent with international literature, as it has been shown that suicide rates were also high for the elderly at three and six years after a SA and that older age is a risk factor for suicide among suicide attempters (Hepple and Quinton, 1994; Lebret et al., 2006; Parra-Uribe et al., 2017). Interestingly, while neurocognitive disorders, physical illnesses, and physical and psychological pain are well-known risk factors for suicidal behavior among the elderly (Conejero et al., 2018; Conwell, 2014; Conwell et al., 2011), in the years following a SA, the elderly had higher rates (from 3- to 7-fold) of deaths from causes other than suicide (Hepple and Quinton, 1994; Wiktorsson et al., 2011).

According to our results, a lower one-year rate of death by suicide was found when participants were people with a first SA. It has been demonstrated in several cohort studies of suicide attempters that having more than one previous SA was a risk factor for a suicide reattempt (Irigoyen et al., 2019; Suokas and Lönnqvist, 1991).

Moreover, we found that the one-year suicide rates was almost half when the method used for the index SA was self-poisoning. The lower rates could be explained by a lower risk of repetition after self-poisoning compared to other methods, as has been found in a Swedish study (Runeson et al., 2010).

Finally, for serious SAs, the rate of subsequent death by suicide was higher at 10 years than for nonserious SAs. In the current literature, violent and serious SAs were also more likely to be associated with a higher risk of repetition (Giner et al., 2014; Runeson et al., 2010).

### Strengths and limitations

Our study is, to our knowledge, the first meta-analysis on suicide mortality after a nonfatal SA. Whereas other meta-analyses took into consideration all DSH attempts, we focused on studies specifically analyzing SAs for more consistency in epidemiology. One of the strengths of our study is the inclusion of studies that focused on specific age groups, specific psychiatric diagnoses and the inclusion of studies regardless of the method used for the index

attempt and the participant inclusion setting. Second, we performed subgroup meta-analysis to take into consideration these specificities and to assess their weight in the suicide rate estimates. Moreover, another strength is the absence of publication bias assessed through funnel plots.

One of the limits of our results is the small number of studies found, the small sample sizes of the studies and the high between-study heterogeneity. Therefore, we performed sensitivity analysis, but heterogeneity was persistent after removing the outliers from the analysis at one and five years. The high level of heterogeneity between the included studies is a significant limitation to the interpretation of the results and particularly to the estimation of the suicide death rate. Nevertheless, a random-effects meta-analysis was used to reduce this bias, and we did not find any impact of sample size or year of publication in our meta-regression analysis. Second, subgroup meta-analyses were based on a small number of studies rather than two for the assessment of the specific age group rates, psychiatric diagnosis and index methods of SA. We still chose to perform these analyses to encourage future research, but results must be interpreted with caution. Third, meta-regression on the mean age of the participants did not find a significant effect on the one-year suicide rate according to our results. This could be explained by the nonlinearity of the mean ages of the participants and the heterogeneity of the results. Fourthly, the risk of bias was heterogeneous from low to high for the cohort studies. Notably, the definition used to characterize the index SA was not specified or was imprecise in several studies and this constituted a bias. Nevertheless, the study quality was fairly high for the majority of the studies included. Finally, the interaction between risk factors was not examined as we did not have access to individual data from the primary studies and we used summary data provided in the included publications.

## CONCLUSION

In conclusion, while half of patients die during their first suicide attempt, those who survive are a group of subjects with a well-known high risk of suicide (Isometsä and Lönnqvist, 1998; Jordan and McNiel, 2020). Hence, the risk of death by suicide after a failed SA remains very high, especially during the first year and seems to persist for many years. The evidence of a high rate of suicide deaths in the year following nonfatal SAs should prompt prevention systems to be particularly vigilant during this period, especially for people with chronic mood disorder. Moreover, little is known about suicide mortality after SA in specific populations, such as adolescents and the elderly, or according to specific psychiatric diagnoses, and further research is needed. Future studies may more accurately identify participants with higher death rates to improve the current prevention programs.

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Table 1. Description of Studies in the Meta-Analysis.

| Study Authors, Year, reference | Design | Country | Size (N) | Sex-ratio (M/F) | Clinical context | Age (mean ± SD) | Number of deaths by suicide | Study quality |
|---|---|---|---|---|---|---|---|---|
| **Beautrais et al, 2003** | Prospective Cohort study | UK | 302 | 0.9 | Participants with a medically serious SA admitted to ED | 30.4 (13.4) | 5 years= 16 | Good |
| **Bostwick et al, 2016** | Population based Retrospective-prospective Cohort study | USA | 1,490 | 0.6 | Residents of Olmsted County, people with a first SA | 27.9 (14.1) | 1 year= 33 | Good |
| **Brådvik et al, 2003** | Prospective Cohort study | Sweden | 58 | 0.7 | Participants discharged from hospital with a diagnosis of primary severe depression or melancholia | | 1 year= 7<br>5 years= 33 | Good |
| **Cullberg et al, 1988** | Prospective Cohort study | Sweden | 163 | | Psychiatric in- or outpatients | | 5 years= 8<br>10 years= 10 | Good |
| **De Leo et al, 2002** | Prospective Cohort study | Europe | 63 | 0.6 | Participants aged 60 years and over who attended health facilities | 68.3 (6.9) | 1 year= 8 | Good |
| **Gehin et al., 2009** | Survey study | Canada | 65 | 0.2 | Adolescents from 11 to 19 years old admitted to Psychiatric Unit at the Children's Hospital and ED | 14.5 (1.5) | 10 years= 2 | Good |
| **Gibb et al, 2005** | Cohort study | UK | 3,690 | 0.7 | Hospital admissions | | 1 year= 52<br>5 years= 108<br>10 years= 170 | Good |
| **Han et al, 2016** | Cohort study | USA | 2000 | 0.7 | Individuals who participated in the 2008-2012 National Surveys on Drug Use and Health | | 1 year= 3.2% | Good |
| **Holley et al, 1998** | Prospective Cohort study | Canada | 876 | 0.61 | People with a first SA admitted to any acute care general hospital | | 10 years= 49 | Good |
| **Hvid et al, 2011** | RCT | Norway | 64 | 0.4 | Admissions to the hospital's ED and clinical departments | | 1 year= 1 | Good |
| **Johnsson Fridell et al, 1996** | Prospective Cohort study | Sweden | 75 | 0.7 | Admissions to the Suicide Research Center | 37 (10) | 1 year= 5<br>5 years= 10 | Good |
| **Kim et al, 2018** | Retrospective Cohort study | Korea | 8,538 | 0.6 | Admissions in ED | 41.2 (17.4) | 1 year= 133<br>3 years= 234 | Good |
| **Kotila et al, 1989** | Cohort study | Finland | 362 | 0.5 | Adolescents between 15 and 19 years old admitted to ED or an ICU | | 5 years= 8 | Fair |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Laurent et al, 1998** | Prospective Cohort study | France | 485 | 0.4 | Adolescents under 18 years old admitted into general and emergency pediatric wards, or pedopsychiatry or clinical toxicology services | 15 (1.9) | 5 years= 5 | Good |
| **Lee et al, 2012** | Prospective cohort study | Taiwan | 102 | 0.5 | Admissions to ED | 37.8 (12.7) | 1 year= 4 | Good |
| **Ligier et al, 2020** | Prospective cohort study | France | 307 | 0.2 | Adolescents under 18 years old admitted to the Nancy Children's Hospital | 14.7 (1.6) | 1 year= 3 | Good |
| **Mäki et al, 2017** | A register-based Cohort study | Finland | 11,606 | 1.3 | Hospital admissions | 43 | 1 year= 487 | Good |
| **Morthorst et al, 2012** | RCT | Denmark | 120 | 0.4 | Participants admitted in acute ED, ICU, pediatric units, and psychiatric emergency rooms | 30.5 (12.1) | 1 year= 0 | Good |
| **Nielsen et al, 1990** | Prospective Cohort study | Denmark | 207 | 1.1 | Admissions in Department of Psychiatry | | 5 years= 24 | Good |
| **Nordentoft et al, 1993** | Prospective Cohort study | Denmark | 974 | 0.7 | Admissions in Poisoning Treatment Centre for self-poisoning | | 10 years= 103 | Good |
| **Nordström et al, 1995** | Cohort study | Sweden | 92 | 0.7 | Participants with mood disorders (major affective disorders, schizoaffective disorder, anxiety disorder or adjustment disorder) | 40 (13) | 1 year= 11 | Good |
| **Nordström et al, 1995** | Prospective Cohort study | Sweden | 1,573 | 0.6 | Admissions to psychiatric emergency room | 37 | 1 year= 43<br>5 years= 90 | Good |
| **O'Donnell et al, 1994** | Prospective Cohort study | UK | 94 | 1.1 | London Underground railway SAs | 40.8 (16) | 10 years= 7 | Good |
| **Ojehagen et al, 1992** | Prospective cohort study | Sweden | 59 | 2.3 | Admissions to medical ICU after a self-poisoning | | 1 year= 2 | Good |
| **Ostamo & Lönnqvist, 2001** | Prospective Cohort study | Finland | 2,782 | 1.0 | Psychiatric and nonpsychiatric patients referred to health care | 37 | 5 years= 157 | Good |
| **Paerregaard, 1975** | Prospective Cohort study | Denmark | 484 | 0.7 | Participants who did a serious SA | | 5 years= 53 | Good |
| **Pallis et al, 1984** | Cohort study | UK | 1,264 | | NA | | 1 year= 12 | Good |
| **Parra-Uribe et al, 2017** | Observational study | Spain | 1,241 | 0.6 | All people with a first SA evaluated in ED | 40.8 (16) | 1 year= 15 | Good |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Pavarin et al, 2014** | Retrospective Cohort study | Italy | 505 | 0.7 | Admissions to ED | 45.6 | 1 year= 11 | Good |
| **Probert-Lindström et al, 2020** | Prospective Cohort Study | Sweden | 1044 | | Admissions to Medical Emergency Inpatient Unit | 40 | 5 years= 40<br>10 years= 56 | Good |
| **Rosen et al, 1976** | Prospective Cohort study | USA | 886 | 0.7 | Patients admitted to regional Poisoning Treatment Center with a medically serious SA | | 1 year= 9<br>5 years= 34 | Good |
| **Skogman et al, 2004** | Prospective cohort study | Sweden | 1,052 | 0.7 | Admissions to Medical Emergency Inpatient Unit | 40 (17) | 1 year= 19 | Good |
| **Steer et al, 1988** | Prospective Cohort study | USA | 499 | 0.7 | Participants hospitalized in general hospital | 30.1 (10.7) | 10 years= 28 | Good |
| **Stenbacka et al, 2015** | Prospective Cohort study | Sweden | 1,195 | | 18–20-year-old young men conscripted for military service from 1969 to 1970 | | 1 year= 69 | Good |
| **Suokas et al, 1991** | Prospective Cohort study | Finland | 1,018 | 0.9 | ED admissions for self-poisoning | | 1 year= 18<br>5 years= 32 | Good |
| **Suominen et al, 2004** | Prospective Cohort study | Finland | 1,198 | 0.9 | ED admissions | 38 | 5 years= 57 | Good |
| **Tejedor et al, 1999** | Prospective Cohort study | Spain | 150 | 0.8 | Psychiatric Department admissions | 41 (18) | 10 years= 18 | Good |
| **Tidemalm et al, 2008** | Prospective Cohort study | Sweden | 39,685 | 0.9 | Hospital admissions | 38.4 (16.5) | 1 year= 1,734 | Good |
| **Vaiva et al, 2018** | RCT | France | 494 | 0.6 | Admissions in ED | 38.1 (13.1) | 1 year= 8 | Good |
| **Weiner et al, 2011** | Retrospective Cohort study | USA | 10,163 | 10.4 | Veterans admitted in medical facilities | 44 (10.8) | 10 years= 1331 | Good |
| **Wiktorsson et al, 2011** | Prospective cohort study | Netherlands | 60 | 0.9 | Participants admitted to ED aged 70 and above | 79.4 (5.4) | 1 year= 2 | Good |

ED= Emergency department; ICU= Intensive care unit

Table 2. Subgroup analysis exploring the incidence of death by suicide after SA on different continents, psychiatric diagnoses, and age groups

| **Analysis** | **One-year incidence** | | | **Five-years incidence** | | | **Ten-years incidence** | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of studies | Incidence (%) | p | Number of studies | Incidence (%) | p | Number of studies | Incidence (%) | p |
| **Overall incidence** | 25 | 2.77 [2.22-3.46] | | 14 | 5.57 [3.88-7.95] | | 11 | 7.39 [5.21-10.38] | |
| **Continent** | | | | | | | | | |
| Europe | 20 | 3.02 [2.40-3.78] | 0.39 | 13 | | | 7 | 7.70 [5.34-10.98] | 0.72 |
| North America | 3 | 2.18 [0.90-5.14] | | 1 | | | 4 | 6.73 [3.45-12.71] | |
| Asia | 2 | 2.18 [0.90-5.14] | | | | | | | |
| **Age group** | | | | | | | | | |
| All | 21 | 2.53 [1.99-3.22] | 0.29 | 12 | 6.59 [4.49-9.50] | <0.01 | 10 | | |
| Adolescents | 2 | 2.61 [0.45-13.75] | | 2 | 1.58 [0.75-3.31] | | 1 | | |
| Elderly | 2 | 7.46 [1.97-24.41] | | | | | | | |
| **Year of publication** | | | | | | | | | |
| Before 2000 | 7 | 2.72 [1.42-5.14] | 0.91 | 8 | 4.58 [2.97-6.99] | 0.24 | 7 | 8.11 [6.15-10.63] | 0.50 |
| After 2000 | 18 | 2.83 [2.20-3.63] | | 6 | 7.21 [3.84-13.12] | | 4 | 6.16 [2.86-12.76] | |
| **Type of study** | | | | | | | | | |
| Cohort study | 22 | 2.88 [2.30-3.62] | 0.05 | 14 | | | 11 | | |
| RCT | 3 | 1.50 [0.80-2.81] | | | | | | | |
| **Method or characteristic of SA** | | | | | | | | | |
| All methods | 21 | 3.00 [2.36-3.80] | 0.07 | 11 | 6.11 [3.93-9.39] | 0.06 | 7 | 6.73 [3.94-11.28] | < 0.01 |
| Self-poisonings | 2 | 1.89 [1.22-2.91] | | 1 | | | 1 | | |
| Serious SA | | | | 2 | 4.29 [3.17-5.79] | | 2 | 10.42 [8.09-13.34] | |
| First-attempters | 2 | 1.71 [0.92-3.18] | | | | | 1 | | |
| **Psychiatric diagnosis** | | | | | | | | | |
| Nonspecified | 23 | 2.45 [1.95-3.07] | <0.01 | 13 | | | 11 | | |
| Mood disorder | 2 | 12.00 [7.69-18.24] | | 1 | | | | | |

SUPPLEMENTARY MATERIALS

Table 1. Meta-regression of moderators/correlates in estimated suicide rates

| | **Moderator** | **N** | **β** | **95% CI** | **p-value** | **$R^2$** |
|---|---|---|---|---|---|---|
| **One-year rate** | | | | | | |
| | Sample size | 25 | 0.000 | [-0.000 - 0.000] | 0.66 | 0% |
| | Year of publication | 25 | 0.0004 | [-0.028 - 0.029] | 0.98 | 0% |
| | Mean age of participants | 16 | -0.0001 | [-0.002 - 0.002] | 0.90 | 0% |
| **Five-years rate** | | | | | | |
| | Sample size | 14 | -0.0003 | [-0.001 - 0.000] | 0.26 | 2.3% |
| | Year of publication | 14 | 0.0101 | [-0.049 - 0.069] | 0.73 | 0% |
| | Mean age of participants | 7 | 0.0623 | [-0.010 - 0.115] | 0.02 | 48.0% |
| **Ten-years rate** | | | | | | |
| | Sample size | 11 | 0.0001 | [-0.000 - 0.000] | 0.26 | 2.9% |
| | Year of publication | 11 | -0.008 | [-0.032 - 0.015] | 0.48 | 0% |
| | Mean age of participants | 6 | -0.001 | [-0.004 - 0.002] | 0.43 | 0% |

Table 2. Critical appraisal checklist.

| Authors | Q 1 | Q 2 | Q 3 | Q 4 | Q 5 | Q 6 | Q 7 | Q 8 | Q 9 | Q1 0 | Q1 1 | Q1 2 | Q1 3 | Critical appraisal score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Beautrais et al, 2003** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Bostwick et al, 2016** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Brådvik et al, 2003** | 2 | 2 | 0 | 0 | 2 | 2 | 1 | 2 | 2 | | | | | 13 |
| **Cullberg et al, 1988** | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 14 |
| **De Leo et al, 2002** | 2 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | | | | | 17 |
| **Gehin et al., 2008** | 2 | 2 | 0 | 2 | 2 | 1 | 2 | 2 | 2 | | | | | 15 |
| **Gibb et al, 2005** | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | | | | | 17 |
| **Han et al, 2016** | 2 | 2 | 2 | 2 | 2 | 0 | 1 | 2 | 2 | | | | | 15 |
| **Holley et al, 1998** | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | | | | | 17 |
| **Hvid et al, 2011** | 2 | 2 | 2 | 0 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 22 |
| **Johnsson Fridell et al, 1996** | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 16 |
| **Kim et al, 2018** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Kotila et al, 1989** | 2 | 2 | 0 | 0 | 2 | 2 | 1 | 2 | 2 | | | | | 10 |
| **Laurent et al, 1998** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 0 | | | | | 16 |
| **Lee et al, 2012** | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 16 |
| **Ligier et al, 2020** | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 16 |
| **Mäki et al, 2017** | 2 | 2 | 2 | 0 | NA | 2 | 2 | 2 | NA | | | | | 12 |
| **Morthorst et al, 2012** | 2 | 2 | 2 | 0 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 22 |
| **Nielsen et al, 1990** | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 13 |
| **Nordentoft et al, 1993** | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | | | | | 18 |
| **Nordström et al,** | 0 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 14 |
| **Nordström et al, 1995** | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **O'Donnell et al, 1994** | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | | | | | 16 |
| **Ojehagen et al, 1992** | 2 | 2 | 0 | 2 | 2 | 0 | 2 | 2 | 2 | | | | | 14 |
| **Ostamo & Lönnqvist, 2001** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 16 |
| **Paerregaard, 1975** | 1 | 1 | 2 | 1 | 2 | 1 | 2 | 2 | 2 | | | | | 17 |
| **Pallis et al, 1984** | 1 | 1 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | | | | | 14 |
| **Parra-Uribe et al, 2017** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Pavarin et al, 2014** | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | NA | | | | | 16 |
| **Probert-Lindström et al, 2020** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Rosen, 1976** | 0 | 1 | 2 | 0 | 2 | 2 | 0 | 2 | 1 | | | | | 18 |
| **Skogman et al, 2004** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Steer et al, 1988** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 16 |
| **Stenbacka et al, 2015** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Suokas et al, 1991** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 16 |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Suominen et al, 2004** | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | | | | | 18 |
| **Tejedor et al, 1999** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Tidemalm et al, 2008** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Vaiva et al, 2018** | 2 | 2 | 2 | 0 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 22 |
| **Weiner et al, 2011** | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | | | | | 18 |
| **Wiktorsson et al, 2011** | 2 | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 0 | | | | | 14 |

*For prevalence studies: Q1: Was the sample frame appropriate to address the target population?; Q2: Were study participants sampled in an appropriate way?; Q3: Was the sample size adequate?; Q4: Were the study subjects and the setting described in detail?; Q5: Was the data analysis conducted with sufficient coverage of the identified sample?; Q6: Were valid methods used for the identification of the condition?; Q7: Was the condition measured in a standard, reliable way for all participants?; Q8: Was there appropriate statistical analysis? Q9: Was the response rate adequate, and if not, was the low response rate managed appropriately?*

*For randomized controlled trials: Q1: Was true randomization used for assignment of participants to treatment groups?; Q2: Was allocation to treatment groups concealed?; Q3 : Were treatment groups similar at the baseline?; Q4 : Were participants blind to treatment assignment?; Q5: Were those delivering treatment blind to treatment assignment?; Q6: Were outcome assessors blind to treatment assignment?; Q7: Were treatment groups treated identically other than the intervention of interest?; Q8: Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?; Q9: Were participants analyzed in the groups to which they were randomized?; Q10: Were outcomes measured in the same way for treatment groups?; Q11: Were outcomes measured in a reliable way?; Q12: Was appropriate statistical analysis used?; Q13: Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?*

## 2. Recherche des causes de décès et des facteurs de risque associés après une TS

Dans notre revue de littérature et méta-analyse, nous avons estimé le taux de décès par suicide après une TS à 2,8% à 1 an, 5,6% à 5 ans et 7,4% à 10 ans. Cependant, peu d'études ont finalement été inclues dans la méta-analyse et on retrouvait une grande hétérogénéité dans les études. Nous avons donc tenté de ré-estimer ce taux dans une grande cohorte régionale de suicidants. Au-delà de la mortalité par suicide, nous avons ensuite essayé de déterminer les autres causes de mortalité impliquées dans la surmortalité des suicidants et les facteurs de risque associés à la mortalité. De la même manière, les précédentes études s'étaient intéressées aux causes de mortalité après un passage à l'acte auto-agressif. L'objectif de cette quatrième étude était donc de déterminer les causes de décès, les taux de décès et les facteurs de risques associés dans une grande cohorte de patients suicidants.

Pour cela, nous disposions d'une cohorte prospective de 7406 suicidants inclus dans les Hauts-de-France, entre 2017 et 2018, dans le dispositif Vigilans. Le dispositif Vigilans, à l'image de l'étude ALGOS, est un dispositif de veille post-hospitalière des patients suicidants reprenant un algorithme similaire (81). Cependant, tous les patients amenés aux soins après une TS étaient inclus dans le dispositif Vigilans quel que soit leur âge ou le lieu de consultation ou d'hospitalisation. Le statut vital des 7406 participants a été recherché grâce aux bases de mortalité de l'INSEE. Ensuite, la cause de décès était recherchée par un appel téléphonique au médecin ou psychiatre traitant du patient décédé. Enfin, l'association entre les facteurs sociodémographiques et cliniques et le risque de décès à 1 an (par suicide ou de toute cause confondue) était recherché.

Selon nos résultats, 125 patients sont décédés (1,7%) dont 77 par suicide (1%) dans l'année suivant une TS. La moitié des décès survenaient dans les 4 premiers mois. Hormis le suicide, les décès de cause cardio-vasculaire (23 sujets), puis des cancers (6 sujets) et des accidents (6 sujets) étaient les causes les plus fréquentes. Enfin, le sexe masculin et l'âge supérieur à 45 ans étaient deux facteurs de risque de décès par suicide ou de décès toute cause confondue. Cette étude met donc en évidence un taux élevé de décès par suicide dans l'année suivant une TS même s'il est bien inférieur à celui estimé dans notre méta-analyse. Les causes cardio-vasculaires apparaissent comme étant la deuxième cause de décès dans cette population. La prévention du suicide est donc particulièrement importante pour les suicidants mais la prise en charge des comorbidités physiques est également primordiale si l'on souhaite diminuer la surmortalité des suicidants.

Article 4. Suicide et mortalité de toute cause dans l'année suivant une TS dans la cohorte Vigilans.

Cet article est actuellement en révision au Journal of Clinical Psychiatry.

# Suicide and all-cause mortality within one year after a suicide attempt in the Vigilans-cohort.

Alice DEMESMAEKER[1]* (MD, MSC), Ali AMAD[1] (MD, PhD), Emmanuel CHAZARD[2] (MD, PhD), Anne-Laure DEMARTY[1] , Honorine SCHLIENGER[1] (MD), Emma LEHMANN[1] (MD), Christophe DEBIEN[1] (MD), Vincent JARDON[1] (MD), Karim BOUNEBACHE[4] , Gregoire REY[4] (MD), Guillaume VAIVA[1,3] (MD, PhD)

1. Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, F-59000 Lille, France
2. ULR 2694 Metrics, CERIM, Public Health Department, CHU Lille, Université de Lille, Lille, France
3. Centre national de ressources et de résilience (CN2R), F-59000 Lille, France
4. INSERM, Centre of Epidemiology on the medical causes of death (CepiDC), Le Kremlin-Bicêtre, France

*Corresponding Author
Dr Alice DEMESMAEKER (MD, MSC)
Hôpital Fontan, CHU de Lille, F-59037, Lille cedex, France
Email: alice.demesmaeker@chu-lille.fr
Tel: + 33 3 20 44 42 15 Fax: +33 3 20 44 62 65

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Main text: 3385 words
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## ABSTRACT

OBJECTIVE: Obtaining better knowledge on what becomes of suicidal patients is crucial for suicide prevention. The aim of our study was to determine the causes of death one year after a suicide attempt (SA) in the VigilanS program, mortality rates, and risk factors associated with any cause of death and suicide.

METHOD: A prospective cohort of 7406 people who had attempted suicide between 2017 and 2018 was included in the study. The vital status of each participant was sought, and the cause of death was established through a phone call to their general practitioner or psychiatrist. Second, the relationship between sociodemographic and clinical factors and death by suicide within one year of a SA was assessed using a multivariable Cox model.

RESULTS: At one year, 125 (1.7%) participants had died, 77 of whom died by suicide. Half of the deaths occurred within the first 4 months after a SA. Hanging (20.3%) and self-poisoning (19.5%) were the methods the most often used for suicide. We demonstrated that male sex (HR=1.79 [1.13 - 2.82], p=0.01) and being older than 45 years old (between 45 and 64 years old HR=2.08 [1.21 - 3.56], p<0.01; above 65 years old HR=5.36 [2.72 - 10.54], p<0.01) were associated with a higher risk of death by suicide one year after a SA and that being younger than 25 years old was associated with a lower risk (HR=0.22 [0.07 - 0.76], p=0.02).

CONCLUSION: One person out of one hundred people who attempt suicide died by suicide within one year after a SA. Greater vigilance is required in the first months following a SA, especially for males older than 45 years old.

Keywords: Suicide attempt, mortality, suicide, epidemiology

# INTRODUCTION

Suicide is a leading cause of avoidable death worldwide, with approximately 700,000 deaths per year [1]. Moreover, with at least 16 million per year, suicide attempts (SAs) are estimated to be 25 to 50 times more common than deaths by suicide. However, even if scientific literature has investigated the relationship between sociodemographic and clinical factors and the risk of death by suicide, the trajectory of people who have attempted suicide remains unclear [2].

In this context, most studies have focused on the rate of death by suicide, as suicide is one of the preventable and well-known causes of death after a SA. Therefore, a recent meta-analysis estimated high rates of death by suicide after a SA (i.e., 2.8% at one year, 5.6% at 5 years, and 7.4% at 10 years) [3]. Nonetheless, while most deaths after an attempt are probably due to natural causes and not to suicide, few studies have precisely examined the cause-specific distribution of post-SA mortality [4,5]. These few studies have divided the causes into natural, external (suicide, accidents, homicides), and uncertain causes [6,7]. In addition, most studies have included a relatively high number of undetermined causes of death (e.g., 5% in a Swedish cohort study, 17.5% in a French register-based study, up to 36% in a Canadian cohort study) or have classified them as suicides [4,8–12]. In summary, the current data and literature lead to many uncertainties and imprecisions regarding the outcomes of patients after a SA.

The literature is more accurate regarding the outcomes of patients who engage in deliberate self-harm (DSH), which includes self-injuries without suicidal intent and SAs [13,14]. After DSH, most natural deaths seem to be due to diseases of the circulatory system, digestive system, and neoplasms [15]. However, the epidemiology, rates and causes of death after any SA and DSH are probably not similar. Obtaining better knowledge on what becomes of suicidal patients, and therefore determining the most at-risk periods and associated risk factors is crucial for suicide prevention.

Every year, approximately 10,000 people die by suicide in France [16]. While the rates of suicide have been declining in recent decades, it remains a major public health issue in our country [17]. Recently, the VigilanS suicide prevention program was created to provide a brief contact intervention and to follow-up patients after hospital discharge for a SA [18]. Patients are included in the program regardless of their psychiatric diagnosis, age, or inclusion location.

Aims of the study

The aim of our study was to determine the causes of death one year after a SA, mortality rates, and risk factors associated with any cause of death and suicide using a cohort from the VigilanS program.

## METHODS

### Study Design

A prospective cohort of 7406 subjects was included in the study between 1 January 2017 and 31 December 2018. All the subjects admitted to health care services in the Hauts-de-France region for a SA were included in the VigilanS brief contact intervention program.

VigilanS is a brief contact intervention combining resource cards, telephone calls and mailings for patients who committed a SA[18]. All attempters received a resource card at inclusion. Those with a history of a prior SA received a phone call within ten days after the attempt. Finally, all attempters received a phone call at 6 months after the SA. The intervention was conducted by a team of mental health care professionals specially trained in suicidal crisis management from the University Hospital of Lille. The included patients were men and women, regardless of age, who had survived a SA. The suicidal intent of the act was evaluated by a psychiatrist before inclusion during an interview. A suicide attempt was considered as ""a situation in which a person has performed an actually or seemingly life-threatening behavior with the intent of jeopardizing his life, or to give the appearance of such an intent, but which has not resulted in death"[19]. Subjects were excluded from the study if they refused to participate or if they died during the index hospital stay.

The VigilanS study was authorized by the French Ministry of Health and approved by the Ethics Committee of the Nord-Pas-de-Calais region, the Commission Nationale Informatique et Liberté (CNIL) and the Local Data Protection Service. In accordance with this legal status, professionals ensure the patient's compliance after complete oral and written information is given, and no signed informed consent is required. It was registered with ClinicalTrials.gov (NCT03134885).

### Data collection

At inclusion, data on sociodemographic characteristics (age, sex), the method of the SA (poisoning, cutting or piercing, hanging, drowning, jumping from a height, use of a firearm), whether the SA was associated with acute alcohol use or medication overdose and the history of prior SAs were collected for each patient. The inclusion location (intensive care unit (ICU), general hospital wards, or other locations (emergency department, psychiatric department, paediatrics department)) was also pointed out to assess the severity of the SA. The SA was considered serious if the patient was hospitalized in the ICU or general hospital wards following the attempt. The name of their general practitioner or psychiatrist was collected.

From March 2019 to January 2020, the vital status of all patients at one year was sought through letters sent to the town halls of birth and residence and to the patients' general practitioners (see Supplementary Materials, Figure 1). Since January 2020, the online availability of the French national mortality database by the French National Institute for Statistical and Economic Studies (INSEE) has permitted us to check the one-year vital status of all patients in the cohort and to determine the eventual dates of death.

Finally, for the patients who died within one year after inclusion, the cause of death was first established through a phone call to their general practitioner or psychiatrist, as a large number of causes of death are unspecified in the French mortality database[8]. When the cause of death remained undetermined, the national French death register "CépiDc" was consulted to find the last cause of death.

Primary and secondary outcomes

The primary outcome was death by suicide within one year after inclusion. The secondary outcome was any cause of death within one year.

Statistical analysis

Descriptive analysis

Descriptive statistics were calculated for the variables of interest. Continuous variables are presented as the means and standard deviations (SDs). Discrete variables are expressed as frequencies and percentages. For patients whose vital status was known, Kaplan–Meier curves were used to represent time from the index SA to death by any cause or suicide. For those who died by suicide, survival curves were also stratified according to sex and age group of the participants.

Analysis of the primary outcome

First, the rate of death by suicide at one year was computed. Then, the age-standardized incidence rate of deaths by suicide per 100,000 person-years (pys) based on the European population was calculated [20]. Second, the relationship between sociodemographic factors (age, sex), clinical factors (the inclusion location, method used for the SA, duration of hospitalization), and death by suicide within one year was assessed using a bivariate Cox model. Other causes of death were considered censored. Then, variables with a p value $< 0.2$ in the previous analysis were included in a multivariable Cox model, and p values $< 0.05$ were considered significant [21,22]. The factors associated with all-cause mortality were considered as

the secondary outcomes and evaluated with the same method. R software version 3.6.1 was used for all analyses.

Sensitivity analysis

The relationship between sociodemographic and clinical factors, and death by suicide within one year was assessed using a bivariate and then multivariable Cox model after removing the subjects with an unknown cause of death. Then, the association between the first phone call within ten days and death by suicide was assessed with the same method (bivariate and multivariable Cox model).

# RESULTS

## Patients at inclusion

A total of 7406 patients were included in our study and followed up for one year (see Table 1). A few numbers of patients (58 patients) were excluded from the study (i.e. refused to participate or died during the index hospital stay). The mean age of the subjects was 38.3 (± 16.4) years old. More than half of the subjects were first-time attempters (53.4%) and women (61.4%). Most of the patients (71.4%) were admitted to emergency departments, psychiatric departments or paediatric departments after their SA. A few of them were admitted to intensive care units (3.3%), and a quarter were admitted to general hospital wards (25.3%). Self-poisoning was the most often used SA method (78.9%), and half of the SAs were associated with acute alcohol use (47.1%).

Insert Table 1 about here.

## Causes of death within one year

One year after a SA, of 7406 patients, 125 (1.7%) died, 77 (1.0%) of whom had committed suicide (see Figure 1). Four causes of death (3.2%) remained unknown at the end of the study. Suicide was the most frequent cause of death in our cohort (77 of 125 patients (61.6%)), followed by circulatory diseases (19.5%) (see Supplementary Materials, Table 1). Among those who died by suicide, a third used poisoning and another third used hanging as the suicide method. In another third of the patients, the method used for suicide remained unknown. The mean age of those who died by suicide was 51.8 (±16.5) years old. Half of them were between 45 and 64 years old (50.6%) and were first-time attempters (50.6%) at inclusion.

While the crude incidence rate of death by suicide is 1039 per 100,000 pys in our study, the age-standardized suicide rate (based on the European population) was estimated at 1415 per 100,000 pys

Insert Figure 1 about here.

## Survival curve analysis

Among those who died within one year, the survival curves estimated according to any cause of death or suicide are presented in Figure 2. Within one year after a SA, half of the deaths from any cause and from suicide occurred within the first 4 months. Moreover, the all-cause and suicide mortality curves evolved in parallel.

Insert Figure 2 about here.

Almost all people who attempt suicide less than 25 years old had a high survival probability within one year for women and men (see Figure 3). In contrast, men aged over 65 years had the lowest probability of survival at one year (95%).

Insert Figure 3 about here.

Factors associated with the risk of death by suicide within one year

According to the multivariable Cox model, being less than 25 years old was statistically associated with a lower risk of death by suicide within one year (HR=0.22 [0.07 - 0.76], p=0.02) compared to being aged 25 to 44 years (see Table 2). Being between 45 and 64 years old (HR=2.08 [1.21 - 3.56], p<0.01) and being older than 65 years of age (HR=5.36 [2.72 - 10.54], p<0.01), compared to being 25 to 44 years old, were associated with a higher risk of future death by suicide. Male sex was also statistically associated with death by suicide within one year (HR= 1.79 [1.13 - 2.82], p<0.01). The inclusion location and acute alcohol use during the last SA were not statistically associated with death by suicide within one year after adjustment for confounding variables (p>0.05).

Factors associated with the risk of death by any cause within one year

The same variables, i.e., being less than 25 years old, being between 45 and 64 years old, being older than 65 years old and male sex, were associated with mortality from any cause within one year (p<0.05) in the multivariable Cox model.

Insert Table 2 about here.

Sensitivity analysis

The association between the risk factors identified and death by suicide was not modified after removing the subjects with an unknown cause of death (male sex (HR=1.79 [1.13 - 2.81], p=0.01), being less than 25 years old (HR=0.22 [0.07 - 0.76], p=0.02), being between 45 and 64 years old (HR=2.07 [1.21 - 3.56], p<0.01) and being older than 65 years of age (HR=5.35 [2.72 - 10.53], p<0.01). Second, among patients with a history of previous SA, 1610 patients on 3454 accepted the phone call within ten days after the attempt. Accepting the phone call within ten days does not appear to be associated with suicide deaths in bivariate and multivariate analysis (HR=0.63 [0.34 - 1.17], p=0.14; and HR=0.55 [0.30 - 1.02], p=0.06).

DISCUSSION

In this paper, we presented a description of all causes of death in a cohort of 7406 people who attempt suicide. Our study tried to determine the causes, rate of death, and associated factors within one year after a nonfatal SA. During the year of follow-up, of the 7406 subjects admitted to the hospital after a SA, 1.7% died. Half of the deaths occurred within the first 4 months after the SA. Hanging and self-poisoning were the methods most often used for suicide. In addition, we demonstrated that male sex and being older than 45 years old were associated with a higher risk of death by suicide at one year. In contrast, being younger than 25 years old was associated with a lower risk of death by suicide. Nonetheless, our results highlighted that a history of previous SAs, the method used for the SA, and the severity of prior SAs were not associated with death by suicide at one year. Finally, our cohort has almost the same distribution of socio-demographic characteristics (a higher percentage of women and an average age of 38 years) and clinical features (a half of first-time attempters, few serious attempts) as the other studies on natural cohorts of suicide attempters admitted to emergency departments or hospital [3].

We estimated a rate of all-cause mortality of 1.7% at one year after a SA. Past studies exploring the outcomes of people who attempt suicide found an all-cause excess mortality in comparison to the general population and more specifically for deaths due to suicide, accidents and cardiovascular diseases [4,5,23]. Premature mortality due to physical health conditions could be explained by the interaction of lifestyle risk factors and poorer physical health care in people who attempt suicide [5,24]. In addition, the current scientific literature seems to estimate higher mortality rates for people who attempt suicide admitted to emergency departments or hospitals, ranging from 2.6% to 6.8% [25–27]. Nonetheless, the mortality rates were higher for men and increased with age.

We determined that the incidence rate of death by suicide was 1.0% at one year after a SA. For patients admitted to emergency departments or hospitals after a SA, recent cohort studies found rates of death by suicide at one year ranging from 1.4% to 4.4% [11,25–28]. Moreover, in 2021, a meta-analysis found a rate of death by suicide of 2.8% [2.2 - 3.5] one year after a nonfatal SA [3]. Surprisingly, our results are lower than expected given the higher incidence of suicide in the Hauts-de-France region [16]. The lower rate of death by suicide in our study could be explained by the effectiveness of the VigilanS brief contact intervention for people who attempt suicide but also by the variety of inclusion locations, average younger age, and the slightly higher proportion of women in comparison to previous studies [29]. However, direct standardization based on a European population estimated a higher incidence of suicide (1,415

per 100,000 pys), which remains low but comparable to other studies. In our study, one-third of those who died by suicide used self-poisoning or hanging, but 32.1% of the suicide methods used remained unknown. In comparison, previous studies highlighted that violent means were most often used for completed suicide (in particular, hanging), and poisoning was used in less than one-third of cases [30–32].

Regarding the most at-risk period, half of the deaths from all-cause mortality and suicide seemed to occur during the first 4 months after a SA. According to scientific literature, the same results were determined with the highest all-cause mortality rates in the first month following a SA [4,25,26,32]. This is partly explained by the fact that most suicide cases seem to occur within the first 6 months after a SA, with the highest risk occurring immediately after the SA [10,25,32]. We can hypothesize that the ongoing suicide crisis and the lack of medical care after a SA, particularly for depression, increase the risk of suicide [33]. In addition, a pre-existing physical illness or functional disabilities may increase the risk of SAs, and/or dysregulation of the stress axis after an attempt may increase the risk of accidents or natural deaths [4,23,34].

According to our results, adolescents had a lower risk of death by suicide within one year after an attempt, but people older than 45 years old and males had a higher risk. Our results are in accordance with scientific literature, as past studies have already noticed that being an adolescent was associated with a lower risk of death by suicide after a SA and that older age and male sex were associated with an increased risk [8,26,28,35–37]. Moreover, male sex and older age were also identified as risk factors for all causes of death among people who attempt suicide, as we noted [4].

Notably, our results did not find an association between the method used for the last SA or the severity of a SA and future death by suicide within one year. In comparison, a Swedish study determined that those who used hanging, strangulation, or suffocation as the SA method were at higher risk of later suicide [31]. Commonly, serious SAs and the use of violent methods for SAs (hanging, suffocation, strangling and jumping from a height) were identified as risk factors for further suicides [28,31,32,38–40]. Our results may be due to the variety of our inclusion locations and the increased vigilance provided by our brief contact intervention program for those who attempted suicide with the use of a violent method or who had a serious SA.

In addition, while our study did not find an association between a history of previous SAs and death by suicide within one year, previous studies found a strong association with suicide repetition and subsequent death by suicide [4,9,32]. Nonetheless, a Spanish study published in 1999 found that the number of previous attempts increased the risk of reattempts but decreased the risk of subsequent suicide [41].

Strengths and limitations

One of the strengths of our study is the exhaustive analysis of causes of death through phone contact with general practitioners and/or the verification of death certificates for all persons who died within one year after a SA. Second, only 3% of causes of death remained unknown at the end of the study. The strong association between the risk factors identified and death by suicide was not modified by these subjects in the sensitivity analysis. Moreover, our study was based on an unselected cohort of people who attempt suicide of the Hauts de France region regardless of sex, age, SA method, or psychiatric diagnosis, which limits the selection bias. Finally, simple clinical features were assessed at inclusion, and their impact on eventual death by suicide was assessed. The identification of risk factors may allow the implementation of a targeted prevention of the population at risk: men over 45 years of age in brief contact interventions. In addition, greater vigilance is required for these subjects at higher risk of death by suicide when the clinician initiates care after a SA.

One of the limitations of our study is that psychiatric diagnosis is not assessed at inclusion in the VigilanS program. Therefore, the strong association between the coexistence of a psychiatric disorder and a SA and the overall risk for suicide could not be analysed. Second, we observed other causes of death besides suicide during the follow-up. Indeed, a death from another cause than suicide could precludes the occurrence of suicide. This may constitute a bias and competing risk models could have been used.

## CONCLUSION

According to our findings, one person in one hundred people who attempt suicide died by suicide within one year after an attempt in the VigilanS program. Greater vigilance is required in the first months following a SA, especially for males older than 45 years old. While suicide is the most common cause of death after a SA, the treatment of physical health conditions should not be neglected. The highlighting of simple sociodemographic and clinical factors associated with mortality is a first step in the improvement of current suicide prevention programs and is necessary to provide targeted interventions.

CLINICAL POINTS:

- What becomes of patients who have attempted suicide is actually unclear. In this prospective cohort of 7406 people who had attempted suicide, 125 (1.7%) participants had died, 77 of whom had committed suicide at one year
- Male sex and being older than 45 years old were associated with a higher risk of death by suicide, and that being younger than 25 years old was associated with a lower risk
- Greater vigilance is required following a suicide attempt, especially for males older than 45 years old

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# TABLES AND FIGURES

**Table 1. Baseline characteristics of the participants.** *([a] Emergency departments, psychiatric departments, paediatric departments)*

| Characteristics | All Patients (N = 7406) N (%) | All deaths (N=125) N (%) | Deaths by suicide (N=77) N (%) |
|---|---|---|---|
| Age (mean ± SD) | 38.3 (± 16.4) | 55.2 (±17.0) | 51.8 (±16.5) |
| < 25 Y | 2004 (27.1) | 3 (2.4) | 3 (3.9) |
| 25–44 Y | 2544 (34.4) | 26 (20.8) | 20 (26.0) |
| 45–64 Y | 2440 (32.9) | 61 (48.8) | 39 (50.6) |
| > 65 Y | 418 (5.6) | 35 (28.0) | 15 (19.5) |
| Women | 4548 (61.4) | 58 (46.4) | 35 (45.5) |
| Men | 2858 (38.6) | 67 (53.6) | 42 (54.5) |
| First-attempters | 3952 (53.4) | 63 (50.4) | 39 (50.6) |
| Inclusion location | | | |
| Other departments[a] | 5279 (71.4) | 38 (30.4) | 18 (23.4) |
| General hospital wards | 1867 (25.3) | 5 (4.0) | 5 (6.5) |
| Intensive care unit | 242 (3.3) | 82 (65.6) | 54 (70.1) |
| Method of the SA | | | |
| Poisoning | 5840 (78.9) | 92 (73.6) | 57 (74.0) |
| Cutting or piercing | 615 (8.3) | 12 (9.6) | 7 (9.1) |
| Hanging | 388 (5.2) | 5 (4.0) | 4 (5.2) |
| Jumping from a height | 130 (1.8) | 4 (3.2) | 2 (2.6) |
| Drowning | 50 (0.7) | 2 (1.6) | 1 (1.3) |
| Use of a firearm | 34 (0.5) | 0 | 0 |
| Other | 349 (4.7) | 10 (8.0) | 6 (7.8) |
| SA with drug overdose | 6026 (81.4) | 95 (76.0) | 60 (77.9) |
| SA with acute alcohol use | 3493 (47.1) | 68 (54.4) | 45 (58.4) |

**Figure 1. Cause of death within one year after an SA (N=125) (A) and the method used for suicide (B).**

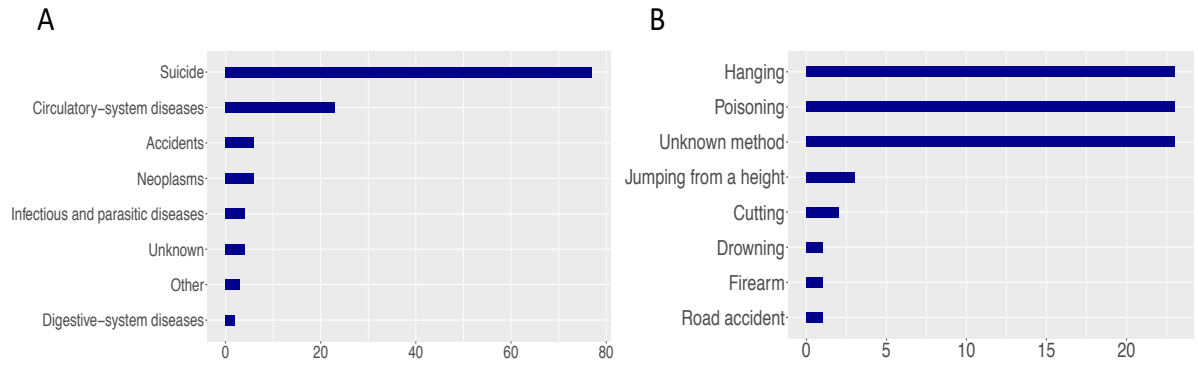



**Figure 2. Kaplan–Meier curves of all-cause and suicide mortality within one year.**

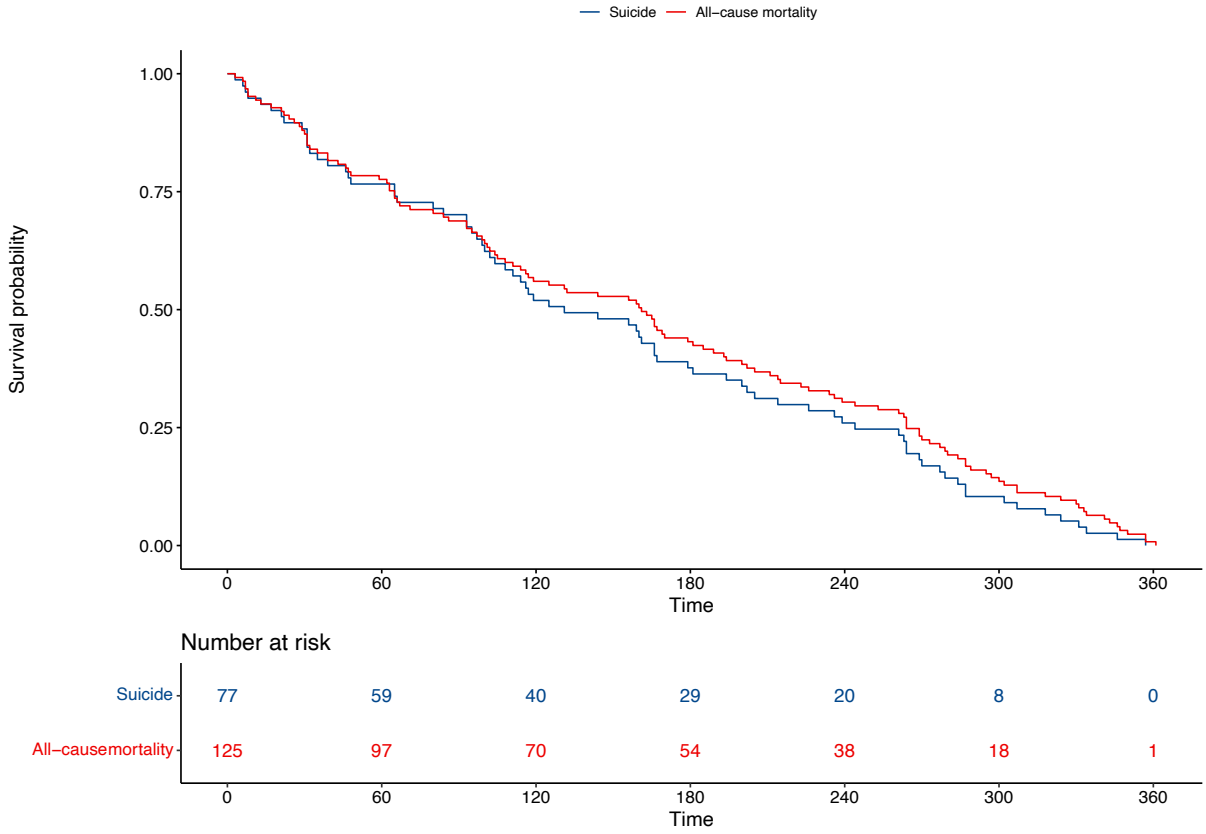


**Figure 3. Death by suicide within one year in women (A) and men (B) according to age group.**

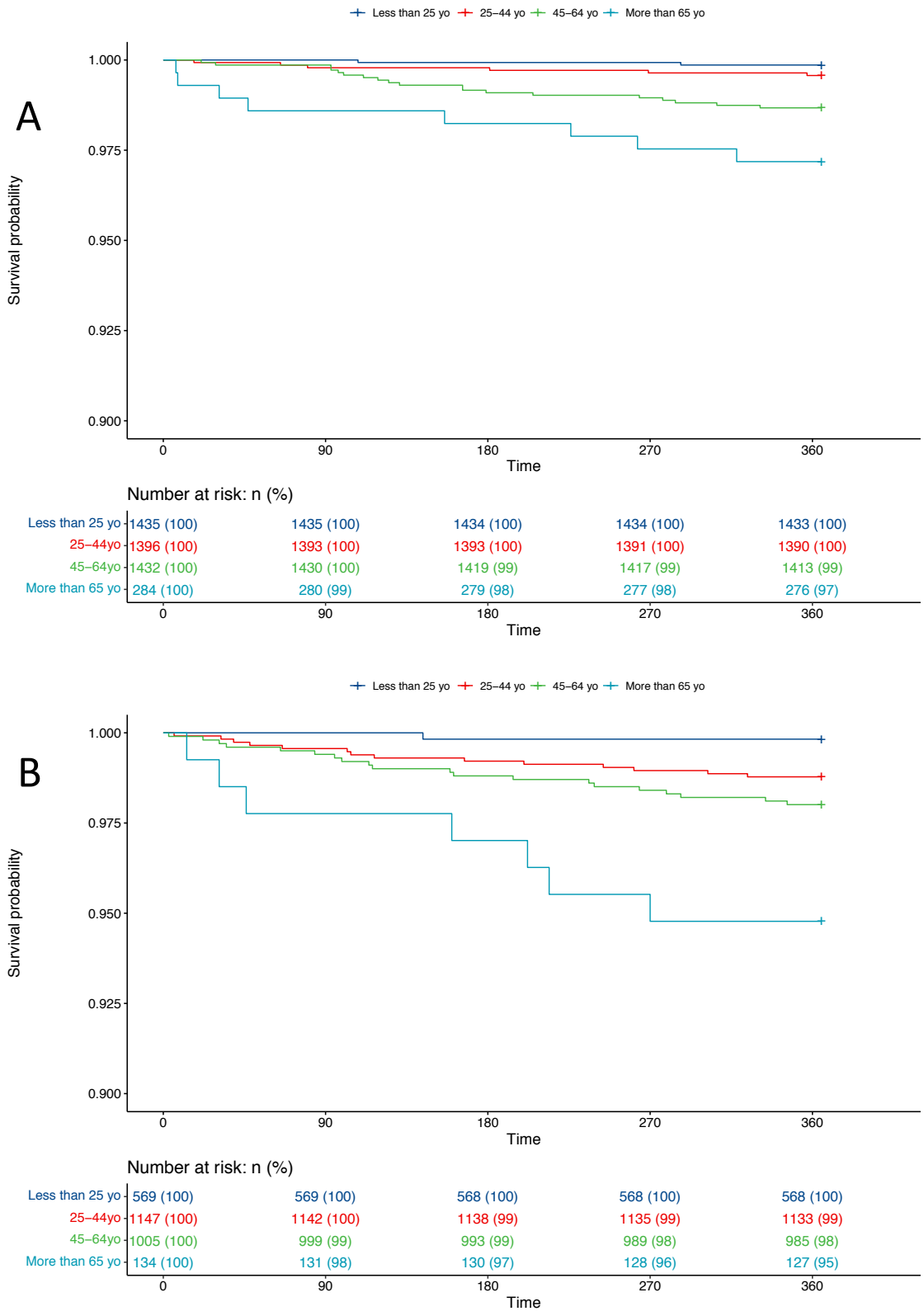


**Table 2. Association between clinical factors and all-cause or suicide mortality within one year.** *([a] Hazard ratio and p value estimated by bivariate Cox model; [b] Adjusted hazard ratio and p value estimated by multivariate Cox model)*

| Factor | Suicide Mortality (N=77) | | | | All-cause Mortality (N=125) | | | |
|---|---|---|---|---|---|---|---|---|
| | HR (95% CI)[a] | P[a] | Adjusted HR (95% CI)[b] | P[b] | HR (95% CI)[a] | P[a] | Adjusted HR (95% CI)[b] | P[b] |
| **Age (ref= 25–44 y)** | | | | | | | | |
| **< 25 Y** | 0.19 [0.05 - 0.64] | <0.01 | 0.22 [0.07 - 0.76] | 0.02 | 0.14 [0.04 - 0.48] | <0.01 | 0.16 [0.05 - 0.52] | <0.01 |
| **45–64 Y** | 2.05 [1.19 - 3.51] | <0.01 | 2.08 [1.21 - 3.56] | <0.01 | 2.46 [1.55 - 3.90] | <0.01 | 2.54 [1.61 - 4.02] | <0.01 |
| **> 65 Y** | 4.76 [2.43 - 9.29] | <0.01 | 5.36 [2.72 - 10.54] | <0.01 | 8.56 [5.15 - 14.21] | <0.01 | 9.40 [5.61 - 15.75] | <0.01 |
| **Male sex** | 1.92 [1.23 - 3.09] | <0.01 | 1.79 [1.13 - 2.82] | 0.01 | 1.85 [1.30 - 2.63] | <0.01 | 1.82 [1.26 - 2.61] | <0.01 |
| **First-time attempter** | 0.90 [0.57 - 1.40] | 0.63 | | | 0.89 [0.62 - 1.26] | 0.50 | | |
| **Inclusion location (ref=Other)** | | | | | | | | |
| **General hospital wards** | 2.13 [0.79 - 5.75] | 0.13 | 2.09 [0.77 - 5.64] | 0.14 | 1.01 [0.40 - 2.57] | 0.98 | 1.06 [0.42 - 2.71] | 0.90 |
| **Intensive care unit** | 1.06 [0.62 - 1.80] | 0.84 | 1.17 [0.68 - 2.00] | 0.57 | 0.76 [0.52 - 1.12] | 0.16 | 0.88 [0.60 - 1.31] | 0.54 |
| **Method of the SA (ref= poisoning)** | | | | | | | | |
| **Cutting or piercing** | 1.17 [0.54 - 2.57] | 0.69 | | | 1.25 [0.68 - 2.28] | 0.47 | 1.39 [0.43 - 4.46] | 0.58 |
| **Hanging** | 1.05 [0.38 - 2.90] | 0.92 | | | 0.82 [0.33 - 2.01] | 0.66 | 0.66 [0.15 - 2.91] | 0.59 |
| **Jumping from a height** | 1.59 [0.39 - 6.51] | 0.52 | | | 1.97 [0.72 - 5.36] | 0.18 | 2.79 [0.62 - 12.55] | 0.18 |
| **Drowning** | 2.05 [0.28 - 14.79] | 0.48 | | | 2.54 [0.62 - 10.31] | 0.19 | 1.25 [0.19 - 8.20] | 0.81 |
| **Use of a firearm** | NC | | | | NC | | NC | |
| **SA with AAU** | 1.58 [1.00 - 2.48] | 0.05 | 1.23 [0.77 - 1.96] | 0.38 | 1.34 [0.94 - 1.91] | 0.10 | 1.04 [0.73 - 1.50] | 0.81 |
| **SA with medication overdose** | 0.80 [0.47 - 1.37] | 0.43 | | | 0.72 [0.48 - 1.09] | 0.12 | 0.95 [0.28 - 3.29] | 0.94 |

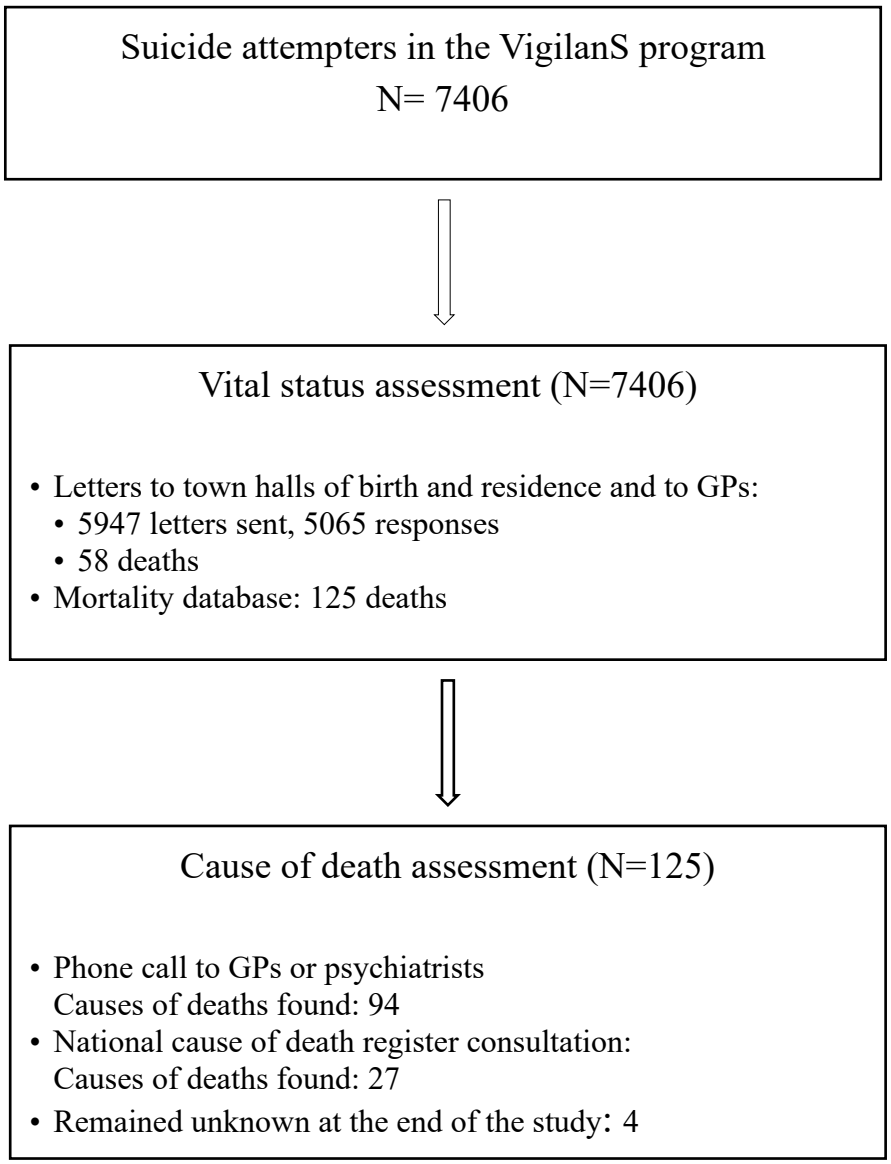
*AAU= Acute alcohol use ; ICU= Intensive care unit ; p = p value*

SUPPLEMENTARY MATERIALS

**Supplementary Table 1. Cause of death within one year after an SA (N=125).**

| Cause of death | n (%) |
|---|---|
| Circulatory-system diseases | 23 (19.5) |
| Neoplasms | 6 (5.1) |
| Accidents | 6 (5.1) |
| Infectious diseases | 4 (3.4) |
| Unknown cause | 4 (3.4) |
| Digestive diseases | 2 (1.7) |
| Cause other than suicide | 2 (1.7) |
| Suspected homicide | 1 (0.8) |
| Suicide | 77 (61.6) |
| *Hanging* | 24 (20.3) |
| *Poisoning* | 23 (19.5) |
| *Unknown method of suicide* | 23 (19.5) |
| *Jumping from a height* | 3 (2.5) |
| *Drowning* | 1 (0.8) |
| *Cutting or piercing* | 1 (0.8) |
| *Use of a firearm* | 1 (0.8) |
| *Road accident* | 1 (0.8) |

**Supplementary Figure 1. Supplementary material. Study flow chart**



# III. EVALUATION D'UN DISPOSITIF DE PREVENTION

Dans les deux chapitres précédents, nous avons analysé la morbi-mortalité des suicidants. Parmi ces travaux, trois études s'appuyaient sur des cohortes de suicidants issues de dispositifs de veille post-hospitalière après une TS. Ces dispositifs de veille-post hospitalière sont une des stratégies de prévention du suicide. Nous allons voir dans ce chapitre les stratégies qui ont fait preuve de leur efficacité dans la prévention du suicide et les stratégies pour lesquelles des études supplémentaires sont nécessaires. Ensuite, nous verrons un exemple d'évaluation d'un dispositif de prévention du suicide qui passait par la formation d'agents sentinelles en maison de retraite.

## 1. Les dispositifs de prévention du suicide

Alors que le suicide est un problème majeur de santé publique, il peut être évité grâce à des stratégies de prévention du suicide. Ces stratégies sont de trois types :

- les stratégies universelles qui visent à toucher l'ensemble de la population tel que la restriction de l'accès aux moyens létaux, l'accès aux soins, la prévention en santé mentale, …
- les stratégies sélectives qui ciblent les populations vulnérables : formation de sentinelles, services téléphoniques d'urgence, …
- les stratégies indiquées qui visent les patients ayant des facteurs de risque de suicide ou ayant fait une TS comme les dispositifs de veille post-hospitalière (ALGOS et Vigilans) etc.

Selon les trois revues de littérature de Mann, Zalsman et Riblet, l'éducation des médecins à l'évaluation du risque suicidaire, la restriction de l'accès aux moyens létaux, les programmes de prévention en milieu scolaire, la clozapine, le lithium, le traitement par psychothérapie et pharmacologique de la dépression et les dispositifs de suicide des patients ont montré leur efficacité dans la prévention du suicide (74,82,83).

Il n'y avait pas assez de preuves pour évaluer l'efficacité de la formation des médias, l'éducation du grand public, la formation de sentinelles, les lignes d'assistance téléphonique etc. Des recherches supplémentaires sont donc encore nécessaires pour évaluer le bénéfice de certains dispositifs de prévention. Nous allons donc voir une méthode pour évaluer l'efficacité des formations qui sont dispensées.

## 2. L'évaluation des dispositifs de prévention

L'évaluation de l'efficacité d'une formation en prévention du suicide peut s'effectuer à différents niveaux. Ainsi, À la fin des années 50, Kirkpatrick a mis en avant un modèle d'évaluation des formations basé sur 4 niveaux d'évaluation. Ce modèle peut s'appliquer aux dispositifs de prévention du suicide de cette manière :

- Le premier niveau consiste à évaluer la satisfaction des participants à la formation
- Le deuxième niveau est l'évaluation de l'acquisition de connaissances, compétences et attitudes autour du suicide
- Le troisième niveau évalue le comportement du stagiaire ; la mise en œuvre des comportements de prévention du suicide
- Enfin, le dernier niveau évalue les résultats en termes de réduction du nombre de TS et suicides après la formation

## 3. La formation Terra Séguin

De 2016 à 2018, dans les Hauts-de-France, de agents sentinelles ont été formés à la prévention du suicide en maison de retraite. En effet, les personnes résidant en maison de retraite sont une population spécifique à haut risque de suicide. Au total, 427 agents ont été formés dans 110 maisons de retraite.

La formation était dispensée pendant 14 heures et couvrait l'épidémiologie du suicide (les taux de suicide chez les personnes âgées et les facteurs de risques), la physiopathologie d'une crise suicidaire, l'évaluation de la crise suicidaire à l'aide du RUD (risque, urgence, dangerosité) et la prise en charge de la crise suicidaire. Ainsi, 28 sessions de formation ont eu lieu. Les formateurs travaillaient en binôme et étaient psychiatres ou infirmiers au sein des équipes mobiles de psychogériatrie. Ils avaient eux-mêmes bénéficié de la formation des Pr Terra et Séguin (84).

Une fois la formation dispensée et les agents sentinelles formés, il est important d'évaluer l'efficacité de cette formation dans la prévention du suicide. L'évaluation de la formation Terra Séguin a donc fait l'objet du cinquième et dernier article de cette thèse. Il s'agit d'un exemple d'évaluation d'un dispositif de prévention pour lequel la littérature scientifique manque de preuves pour attester de son efficacité.

## 4. Évaluation de la formation Terra Seguin

L'évaluation de la formation Terra Séguin reposait sur deux études : une évaluation des connaissances des stagiaires et une estimation de la différence des taux de TS et suicide avant et après la formation des agents sentinelles.

La première étude appréciait les connaissances et les représentations sur le suicide (deuxième niveau d'évaluation selon le modèle de Kirkpatrick). Un questionnaire était complété par les participants avant et juste après la dispensation formation afin de déterminer leurs connaissances et leurs représentations sur le suicide. Le questionnaire était issu de "Knowledge of Suicide Scale (KSS)" (85) et de "Stigma of Suicide Scale" (Soss) (86).

Ensuite la deuxième étude était un questionnaire rétrospectif qui était envoyé aux 110 maisons de retraite participantes en novembre 2018. Il tentait de déterminer le nombre de TS et suicides dans les 12 mois avant la formation et dans les mois suivant la formation.

Enfin, un questionnaire de satisfaction était complété par les participants ; il s'agit du premier niveau d'évaluation selon Kirkpatrick.

Nous avons retrouvé une nette amélioration des connaissances et des représentations sur le suicide chez les 315 participants qui ont complété le questionnaire. De plus, une diminution du nombre de TS était observée après la formation dans les maisons de retraite. Toutefois, on n'observait pas de réduction du nombre de suicides en raison du faible nombre de cas.

Cette étude d'évaluation de la formation d'agents sentinelles dans les maisons de retraite démontre une efficacité de ce dispositif dans la réduction du nombre de TS. Bien que cette étude a de nombreuse limites, il s'agit d'une piste prometteuse dans la prévention du suicide.

Article 5. Évaluation de la formation d'agents sentinelles pour la prévention du suicide dans les EHPAD.

Cet article a été publié dans le Journal of Geriatric Psychiatry and Neurology en janvier 2023.


# Assessment of a Suicide Prevention Gatekeeper Training Program for Nursing Home Staff

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Alice Demesmaeker[1,2,3], Nicolas Baelde[3], Ali Amad[1,2,3], Jean Roche[3], Marie Playe[3], Guillaume Vaiva[1,2,3], Alina Amariei[1], Wanda Blervaque[1], Marguerite Marie Defebvre[4], Brigitte Caron[4], Francois Puisieux[5], and Laurent Plancke[1,6]

# Assessment of a suicide prevention gatekeeper training program for nursing home staff.

Demesmaeker A.[1,3,4], Baelde N.[4], Amad A. [1,3,4], Roche J.[4], Playe M.[4], Vaiva G.[1,3,4], Amariei A.[1], Blervaque W., Defebvre M.-M.[5], Caron B.[5], Puisieux F.[6], Plancke L.[1,2]

1. Regional Federation of Research in Psychiatry and Mental Health Hauts-de-France (Fédération régionale de recherche en psychiatrie et santé mentale) Hauts-de-France (Saint-André-lez-Lille, France)
2. Lille Centre of Sociology and Economy Studies and Research (Centre lillois d'études et de recherche en sociologie et en économie) (Lille, France)
3. Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, F-59000 Lille, France
4. University Hospital of Lille, Department of Psychiatry (Lille, France)
5. Regional Health Agency Hauts-de-France (Lille, France)
6. University Hospital of Lille, Department of Geriatary (Lille, France)

Abstract: 250 words
Main text: 2534 words
Tables and Figures: 4 tables

## ABSTRACT

INTRODUCTION: Older adults have one of the highest age-specific suicide rates in France, and the risk of suicide is higher for those living in nursing homes. The aim of our study was to assess the effectiveness of gatekeeper training for nursing home staff on the knowledge and stigmas towards suicidal crisis as well as the impact on suicidal behaviour rates.

METHOD: A total of 427 nursing or administrative staff from 110 nursing homes received gatekeeper training in the Hauts-de-France French region between September 2016 and June 2018. First, knowledge and stigmas on suicidal crisis were assessed through a pretest and posttest survey. Second, a retrospective survey was conducted to determine suicide behaviour rates before and after training in nursing homes. Then, changes between pre- and posttraining scores and suicide rates were evaluated with a paired samples T test and rate difference calculation (p value of $<0.05$ was considered statistically significant).

RESULTS: A total of 315 trainees completed the questionnaires on knowledge and stigmas related to suicidal crisis, and we found a significant difference in the total scores ($p<0.01$). Moreover, we found a significant decrease in the incidence of suicide attempts (SAs) after training ($p=0.002$), but the incidence of deaths by suicide was not significantly different prior to and after the training course ($p=0.46$).

CONCLUSION: We highlighted an improvement in knowledge and stigmas after training and a reduction in the rates of SAs with our gatekeeper suicide prevention program. Future research is needed to improve suicide prevention for nursing home residents.


Keywords: suicide, prevention, gatekeeper, nursing home

# INTRODUCTION

Suicide remains a major public health issue worldwide, with approximately 800,000 deaths per year [1,2]. In France, approximately 8,000 deaths by suicide were recorded in 2016, accounting for 1.5% of all deaths 3. Notably, 31.7% of these deaths occurred among subjects aged over 65 [3]. Indeed, older adults have one of the highest age-specific suicide rates (per 100,000 persons) in France, and the incidence rate of suicide is increasing with age [3]. Similar suicide rates for the elderly were found in other countries around the world (including 16.5 in the United States and 25.5 in Japan among persons aged 70 years and older in 2012) [4]. Moreover, the World Health Organization estimated that worldwide suicide rates were higher for men than for women aged 75 and older [5]. In recent studies, it was suggested that elderly individuals were at greater risk of death by suicide due to the interaction of many factors, such as affective disorders, physical illness and functional impairment caused by degenerative and chronic diseases [6–9].

In 2015, 10% of adults aged 75 and older and one-third of those aged 90 and older were living in long-term care (LTC) facilities in France [10]. Among these subjects, approximately 80% lived in nursing homes for dependent elderly subjects. Recently, a higher risk of death by suicide among older adults living in or transitioning to LTC settings was established [11]. These LTC residents appear to be particularly at risk of death by suicide considering that approximately half of them suffered from depression and their exposure to major life stressors such as health deterioration, isolation, loneliness and maladjustment to nursing home life [12–15].

While suicide risk seems to be high among the elderly in LTC settings, these facilities may, therefore, be important locations for prevention. Living in nursing homes could have a protective effect on suicidal behaviour [16], as they permit 24-hour care and supervision and rapid intervention by staff and/or medical emergency services [13]. Nonetheless, there is currently a paucity of research on suicide prevention programs for nursing home residents [17–19].

According to recent research, gatekeeper training seems to be the most frequently used means of prevention for nursing home residents [20]. Gatekeepers are health care workers who are in contact with individuals at risk of suicide and are trained to assess and manage suicidal behaviour [21]. Nonetheless, while gatekeeper training in prisons and schools resulted in a decrease in suicidal behaviour for prisoners and students, it did not demonstrate a direct effect on suicidal behaviours for nursing home residents [18,20]. Thus, the development and assessment of gatekeeper training strategies for residents living in nursing homes can be considered a major challenge for preventing suicide in the elderly.

The aim of our study was to assess the effectiveness of suicide prevention gatekeeper training in nursing homes on the knowledge and stigmas towards suicidal crisis as well as the impact on suicidal behaviour rates.

## METHOD

A total of 427 nursing home employees received gatekeeper training in the Hauts-de-France region in France between September 2016 and June 2018. This training consisted of a two-day training course of 14 hours that covered the epidemiology (rates of suicide in the elderly people and risk factors associated), pathophysiology of an suicidal crisis, assessment (based on three dimensions: risk, urgency, dangerousness), and management of suicidal crisis with clinical cases and role plays [22]. The trainees were staff members of 110 nursing homes. They were trained during 28 training sessions by nine pairs of trainers composed of psychiatrists or nurses from mobile psychogeriatric units.

### Study design

Two evaluations were performed to assess the gatekeeper suicide prevention program.

### Assessment of knowledge and stigmas towards suicidal crisis

The first longitudinal study consisted of an evaluation immediately prior to training (pre-test) and upon completion of each training session (post-test). Pretest and posttest surveys were completed during the 28 training sessions, from September 2016 to June 2018.

In pre- and posttest surveys, the characteristics of each respondent (age, sex, and profession) were collected. Knowledge and stigmas (i.e. attitudes, beliefs) on suicidal crisis were assessed [21] according to nineteen selected items from the "Knowledge of Suicide Scale (KSS)" [23] and the "Stigma of Suicide Scale" (Soss) [24] (see supplementary materials, Table 1). The items were selected by a panel of experts and the Cronbach alpha coefficient of the scale was 0.7 (knowledge subscale alpha=0.7, stigmas subscale alpha=0.6). The items were scored "not at all", "not really", "a little bit", "absolutely", and "I don't know" or "false", "rather false", "rather true", "true" and "I don't know" on a 5-point Likert scale. Finally, a total score was computed per participant. So, the knowledge scale was rated on 36 and the stigma scale on 40.

### Suicide behaviour rates in nursing homes

Second, a retrospective survey was also conducted in all 110 nursing homes in November 2018 to determine suicide behaviour (i.e. suicide attempts (SAs) and deaths by suicide) rates before and after training in all nursing homes. A suicide attempt was defined as ""a situation in which a person has performed an actually or seemingly life-threatening behavior with the intent of jeopardizing his life, or to give the appearance of such an intent, but which has not resulted in death" [16].

Nursing home administrators had to determine the number of SAs and deaths by suicide recorded by their physicians among their residents in the twelve months prior to training. The rate of suicide attempts and death by suicide were also assessed in the posttraining period (at least six months after the course). The follow-up time was different between nursing homes and the period necessary to complete the surveys. Each nursing home had to collect the date and the type of suicidal behaviour (SA or death by suicide). Since the survey was experiencing time variations in follow-up for the posttraining period, suicide behaviour rates were computed in person-years (PY). The average follow-up time after the training was 15 months. Moreover, the number of residents per nursing home was obtained by the Regional Health Agency.

Satisfaction assessment

Participants' satisfaction with the training was assessed at the end of the training course. They were asked if training seemed important to them, if they were satisfied with the training, if the training was useful, if they understood the points discussed, and finally if they were satisfied with the organization. Answer choices for these items, including "not at all", "not really", "a little bit", "absolutely", and "I don't know", were rated on a 5-point Likert scale.

Statistical Analysis

Descriptive statistics were first calculated for the characteristics of trained staff members, the characteristics of nursing homes, responses of pre/posttest surveys, and suicidal behaviour rates prior to and after training. The results of the satisfaction assessment were also described. Continuous variables are presented as the mean and standard deviations (SD). Discrete variables are expressed as frequencies and percentages.

Second, changes between pre- and posttraining scores for knowledge and stigmas were evaluated with a paired samples T test after imputation of missing data with the multiple imputation method by chained equation [25]. The fifty datasets were generated with all the variables available using the MICE package of R software. Then, a multiple linear regression was computed to assess the effects of age, gender, and job type on the differences in pre/posttest scores and with an adjustment for baseline score.

Finally, changes in the rates of suicide attempts and deaths by suicide prior to and after training for each nursing home were evaluated with the calculation of the incidence rate difference and its 95% confidence interval (CI) [26]. A p value of $<0.05$ (two-tailed) was considered statistically significant for all analyses. R software version 3.6.1 was used for all analyses.

This project was on the evaluation of the knowledge of health professionals. According to the current French legislation, an ethics committee was not required (Law No. 2012–300 of 5 March 2012, relating to research involving Humans, known as the Jardé law) [27]. However, the questionnaires were completed anonymously after obtaining each participant's consent.

## RESULTS

### Assessment of knowledge and stigmas on suicidal crises

Of the 427 trainees, 315 (73.8%) completed the questionnaires on knowledge and stigmas of suicidal crises (see Table 1). The mean-age of participants was 39 (10.3) years old. Most of the participants of the course were females (80.3%) and were employed as nurses (42.5%) and assistant nurses (25.7%). At baseline, staff members showed relatively limited knowledge on suicide and little confidence in identifying suicidal crises (mean score = 14.2 (4.1) out of 36). Approximately 8% of the data were missing for pretest scores, and approximately 10% were missing for sex, age, job type and posttest scores.

We found a significant difference between pre- and posttraining scores on knowledge (mean difference= 8.8 (4.7), $p<0.01$) and stigmas of suicidal crisis (mean difference= 4.4 (5.0), $p<0.01$) (see Table 2).

Table 3 shows the association between the characteristics of participants and the differences in pre/posttest scores in unadjusted analysis and the final adjusted analysis. None of the variables remained significant in the adjusted model assessing the effects of the characteristics of the participants on knowledge improvement. Concerning the stigmas of suicide, two variables (being an assistant nurse or an administrative officer compared to a nurse) were statistically associated with a lower difference in pre/posttest scores ($p<0.05$) after an adjustment for covariates.

Insert Table 1, Table 2, Table 3 about here.

### Suicidal behaviour rates

A total of 72 (65%) of 110 nursing homes completed the second survey. The 72 nursing homes had a total of 6,846 residents. They had an average of 94 residents (ranging from 25 to 368 residents). We reported 31 SAs and 1 death by suicide before training during 6778 PY. The SA rate was 457 SAs per 100 000 PY and 15 suicide deaths per 100 000 PY. In the posttraining period, we recorded 16 SAs and 3 deaths by suicide. Thus, the SA rate was 172 SAs per 100 000 PY and 32 suicide deaths per 100 000 PY.

We found a significant decrease in the incidence of SAs after training (rate difference= -285.8 (95% CI [-467.5; -104.2]), p=0.002) (see Table 4). Nonetheless, the incidence of deaths by suicide was not significantly different prior to and after the training course (rate difference= 17.4 [-29.1; 63.9], p=0.46).

Insert Table 4 about here.

Satisfaction assessment

The satisfaction score was high after training, and all participants (100%) were somewhat satisfied with the theme and the content of the training. They were also somewhat to very satisfied with the usefulness in clinical practice (98.6%), the points addressed (99.3%) and the organization of the course (99.7%).

## DISCUSSION

To our knowledge, this is one of the few studies to assess a gatekeeper program among nursing home staff members. A total of 427 trainees across 110 nursing homes benefitted from our suicide prevention program. Our results showed a significant improvement in knowledge and stigmas concerning suicidal behaviour after training. Moreover, while the incidence of deaths by suicide was not significantly different prior to and after training, the incidence of SAs was significantly lower in the months after training. Participants were also satisfied with the training course.

The results of our pre/post-stage questionnaires highlighted an improvement in knowledge and stigmatization attitudes towards suicidal crisis after gatekeeper training. Although very few studies have focused on gatekeeper training for nursing home staff, our results are in accordance with a previous controlled quasi-experimental study, a German pilot study, and a study on staff working in community hospice settings [28–30]. Gatekeeper training programs have also shown an improvement in knowledge and help-giving behaviours for trainees working with youth and for students [31–33]. Moreover, we found lower differences in pre/posttest scores on the stigma scale for assistant nurses and administrative officers than for nurses. This result may indicate a lower improvement in attitudes towards suicide for these job types. Previous studies showed a better improvement in knowledge about suicide for mental health professionals compared with other occupations, but no study seemed to explore the improvement in attitudes towards suicidal crisis according to job type [34–36].

Notably, our study is the first to examine the association between gatekeeper training and SAs and completions in nursing homes [37]. We found a large decrease in the incidence of SAs in nursing homes after gatekeeper training. These results could be explained by the improvement of self-efficacy on suicidal crisis after training. However, the incidence of death by suicide was too low to assess differences after training. In comparison, a gatekeeper prevention program for high school students in Columbus and another in the Army of Serbia and Montenegro showed a significant decrease in reported SAs after training [38,39].

### Strengths and limits

Our study is one of the first to assess a gatekeeper suicide prevention program for nursing home staff. A high number of nursing homes participated and were satisfied with the training. Moreover, few studies have focused on the association of suicide risk and living in a nursing home, and they have found contradictory results [15]. To our knowledge, this is the first study evaluating the rates of SAs and deaths by suicide after gatekeeper training in nursing

homes. The results are promising with an improvement in knowledge and stigmas towards suicide for all trainees.

One of the limitations of our study is its observational design with the absence of a control group and a standardized follow-up, meaning that the findings cannot show a causal effect of gatekeeper training. Then, the first survey on knowledge and stigmas on suicidal crisis obtained only 74% of responses. Among the responses, we accounted for approximately 10% of missing data. Therefore, statistical analyses were performed on multiply imputed datasets for more robustness. Moreover, the questionnaire used was not standardized but it has been validated by a committee of experts and showed satisfactory internal consistency.

Concerning the second survey, 35% of nursing homes did not answer the survey, and the results must therefore be interpreted with caution. The calculation of the difference in incidence rates does not allow adjustment for potential confounding factors and does not take into account potential site effect. However, the number of beds, the staff ratio and turnover may influence suicidal behaviour [11]. Furthermore, the rate of death by suicide showed a nonsignificant increase after training. This result can be explained by the very small number of completed suicides in the study and a longer average follow-up time after training. In addition, a memory bias is possible as the nursing homes administrators might not remember all the suicidal behaviors that occurred in their facilities. Moreover, the participants and in particular administrative officers have probably better identified and classified suicidal behaviors which could lead to an improved reliability in data recording in the posttraining period.

## CONCLUSION

While suicide rates in nursing homes seem to be high, implementing prevention programs is of major importance. We highlighted an improvement in knowledge and stigmas after training and a reduction in rates of SAs with the “Terra-Seguin” gatekeeper suicide prevention program. Few studies have explored the impact of gatekeeper training for suicide prevention and, more specifically, for nursing home staff, and programs are heterogeneous. Future studies are needed to examine which components yield more promising effects and their impact on suicide behaviour rates.

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# TABLES

Table 1. Characteristics of respondents to pre/post-survey.

| | Participants N (%) |
|---|---|
| ALL | 315 (100.0) |
| Age (mean (SD)) | 39.0 (10.3) |
| <20 | 1 (0.3) |
| 20-29 | 65 (20.6) |
| 30-39 | 86 (27.3) |
| 40-49 | 79 (25.1) |
| 50-59 | 44 (14.0) |
| 60-69 | 7 (2.2) |
| Sex | |
| Male | 31 (9.8) |
| Female | 253 (80.3) |
| Employment | |
| Assistant nurse | 81 (25.7) |
| Nurse | 134 (42.5) |
| Doctor | 25 (7.9) |
| Psychologist | 28 (8.9) |
| Administrative officer | 12(3.8) |

Table 2. Assessment of knowledge and stigmas on suicidal crisis

| | Pretest score | Posttest score | Mean difference* | t | P VALUE* |
|---|---|---|---|---|---|
| Knowledge and self-efficacy: mean (SD) | 14.2 (4.1) | 22.6 (3.1) | 8.8 (4.7) | -31.8 | <0.01 |
| Stigmas: mean (SD) | 27.6 (4.3) | 32.0 (3.9) | 4.4 (5.0) | -15.6 | <0.01 |

*Result of paired samples T test on imputed datasets

Table 3. Association between the characteristics of participants and the differences in pre/post test scores with multivariable linear regression analysis.

| | Unadjusted model estimate | | | | Adjusted model estimate | | | |
|---|---|---|---|---|---|---|---|---|
| | Coef. | SE | t | P value | Coef. | SE | t | p value |
| Knowledge and self-efficacy | | | | | | | | |
| Age (ref= 20-29) | | | | | | | | |
| 30-39 | 0.77 | 0.66 | 1.16 | 0.24 | 0.16 | 0.45 | 0.37 | 0.71 |
| 40-49 | 0.50 | 0.67 | 0.75 | 0.46 | -0.25 | 0.47 | -0.53 | 0.60 |
| 50-59 | 0.58 | 0.81 | 0.72 | 0.47 | -0.43 | 0.57 | -0.75 | 0.46 |
| 60-69 | 0.86 | 1.67 | 0.51 | 0.61 | 0.78 | 1.19 | 0.65 | 0.52 |
| Sex (ref= female) | | | | | | | | |
| male | 0.16 | 0.80 | 0.20 | 0.84 | 0.21 | 0.59 | 0.36 | 0.72 |
| Employment (ref= Nurse) | | | | | | | | |
| Assistant nurse | 1.51 | 0.60 | 2.51 | 0.01 | -0.52 | 0.43 | -1.22 | 0.22 |
| Doctor | -1.56 | 0.91 | -1.70 | 0.09 | 0.55 | 0.63 | 0.87 | 0.39 |
| Psychologist | -1.68 | 0.85 | -1.98 | 0.05 | 0.21 | 0.57 | 0.37 | 0.71 |
| Administrative officer | 1.71 | 1.30 | 1.31 | 0.19 | 0.19 | 0.90 | 0.22 | 0.83 |
| Stigmas on suicide | | | | | | | | |
| Age (ref= 20-29) | | | | | | | | |
| 30-39 | -0.67 | 0.82 | 0.84 | 0.40 | -0.99 | 0.65 | -1.52 | 0.13 |
| 40-49 | -0.13 | 0.81 | -0.16 | 0.88 | -0.86 | 0.66 | -1.30 | 0.19 |
| 50-59 | -0.06 | 0.96 | -0.07 | 0.95 | -1.08 | 0.82 | -1.33 | 0.19 |
| 60-69 | -0.43 | 2.03 | -0.21 | 0.83 | -2.61 | 1.82 | -1.44 | 0.15 |
| Sex (ref= female) | | | | | | | | |
| Male | 0.05 | 0.92 | 0.06 | 0.95 | 0.36 | 0.80 | 0.46 | 0.65 |
| Employment (ref= Nurse) | | | | | | | | |
| Assistant nurse | -0.64 | 0.67 | -0.96 | 0.34 | -1.39 | 0.54 | -2.58 | 0.01 |
| Doctor | -1.60 | 1.05 | -1.52 | 0.13 | -0.06 | 0.93 | -0.07 | 0.95 |
| Psychologist | -2.64 | 0.96 | -2.77 | <0.01 | -0.06 | 0.79 | -0.07 | 0.94 |
| Administrative officer | -2.97 | 1.51 | -1.97 | 0.05 | -3.05 | 1.24 | -2.45 | 0.02 |

Table 4. Number of cases (n), incidence of suicide behaviour rates per 100 000 residents and rate difference prior and after training.

| | Before training | | After training | | Rate difference | p value |
|---|---|---|---|---|---|---|
| | n | Incidence rate | n | Incidence rate | | |
| Suicide attempt | 31 | 457 | 16 | 172 | -285.8 [-467.5; -104.2] | 0.002 |
| Death by suicide | 1 | 15 | 3 | 32 | 17.4 [-29.1; 63.9] | 0.46 |

# IV. DISCUSSION

Actuellement, le nombre élevé de TS et de suicides en France fait de la prévention des TS et du suicide un enjeu majeur de santé publique. Afin d'améliorer les dispositifs de prévention, la mise en évidence de patients particulièrement à risque de récidiver et les périodes les plus à risque est important. Dans ce contexte, la littérature scientifique a identifié une sous-population de patients, les suicidants, qui sont à haut risque de récidive. A travers ce travail de thèse nous avons mis en évidence des facteurs de risque de récidive de TS à l'aide d'approches innovantes, déterminé le taux et les causes de mortalité et notamment par suicide chez les suicidants et donné un exemple d'évaluation d'un dispositif de prévention du suicide.

Ainsi, dans les deux premiers articles de ce travail nous avons pu déterminer des groupes de patients à risque de récidive de TS dans les 6 à 14 mois suivant une tentative. De cette manière, les patients présentant un trouble de l'usage d'alcool et ayant consommé de l'alcool lors de leur dernière TS, ceux ayant un trouble anxieux, les patients qui ont fait plus de deux TS et enfin la consommation de benzodiazépines et/ou d'hypnotiques se sont révélés être des facteurs de risque de récidive dans l'année suivant la TS. Nos résultats sont intéressants à deux niveaux : lors de l'évaluation clinique d'un patient après une TS et dans l'amélioration des dispositifs de prévention. D'abord, à la lumière de nos résultats une vigilance accrue sera apportée aux patients présentant un trouble de l'usage d'alcool, un trouble anxieux ou ayant récidivé plus de deux fois et lors de la prescription de psychotropes. Ensuite, pour les dispositifs de prévention du suicide tel que la veille post-hospitalière, la mise en évidence de sous-groupes à risques permet de cibler ces patients avec des intervention spécifiques telles que le rappel téléphonique précoce ou l'envoi de cartes postales.

Dans la deuxième partie de ce travail, nous avons tenté d'explorer les causes de mortalité chez les suicidants et les taux de mortalité en portant une attention particulière à la mortalité par suicide. Nous avons estimé le taux de mortalité à 1, 5 et 10 ans suivant une TS à l'aide d'une méta-analyse. Le taux de mortalité par suicide était le plus élevé durant la première année suivant la TS et était estimé à 2.8%. Cependant, les résultats doivent être interprétés avec prudence étant donné la grande hétérogénéité des études inclues. Cela nous a incité à réaliser une étude exhaustive des causes de décès après une TS dans une cohorte naturelle de suicidants (la cohorte Vigilans de 2017 et 2018). Nous avons démontré que le suicide était la cause la plus fréquent de décès dans l'année suivant une TS suivie par les causes cardiovasculaires, les cancers et les accidents. Au regarde de nos résultats, la diminution de la mortalité des suicidants ne passe pas uniquement par la prévention du suicide. Une prise en charge globale, à la fois

psychiatrique et physique, est nécessaire. Ce constat avait déjà été établit dans la littérature quel que soit le trouble psychiatrique dont souffrait le patient (1).

Enfin, la formation Terra Séguin qui consistait en la formation d'agents sentinelles dans les maisons de retraite a été évaluée. Nous avons démontré une efficacité de cette formation dans l'amélioration des connaissances et des représentations sur la crise suicidaire chez les participants mais également une diminution du nombre de TS dans les maisons de retraite après la dispensation de la formation. Cette étude est l'une des premières à évaluer l'impact de ce dispositif de prévention sur le suicide. Bien qu'il ne s'agisse pas d'un essai randomisé contrôlé, la mise en évidence d'une efficacité de cette formation à plusieurs niveaux est un début encourageant pour des études ultérieures.

Maintenant que les principaux résultats de ce travail de thèse ont été rappelés, nous allons passer en revue les points forts et les points faibles de notre travail.

En premier lieu, les études effectuées dans ce travail de thèse ont plusieurs points forts. Tout d'abord, un des principaux points forts de cette thèse est notre souci constant d'être précis et constants sur les termes utilisés. En effet, dans la littérature scientifique, on retrouve de nombreux travaux sur le risque de récidive et de suicide après un PAA. Comme nous l'avons vu précédemment, la CIM-11 classe les TS dans les « automutilations intentionnelles ». Les études qui explorent des données de santé codées à l'aide de la CIM-11 ne peuvent donc pas appréhender l'intention suicidaire du geste. De plus, nous avons vu que dans certaines régions, le terme de PAA est préféré aux TS car l'intentionnalité suicidaire d'un geste peut être difficile à établir. Néanmoins, alors que les PAA regroupent les TS et les automutilations sans intentionnalité suicidaire, il nous a paru important de différencier ces deux termes. De cette manière, nous avons démontré que le risque de décès par suicide, dans l'année suivant une TS, est plus important qu'après n'importe quel PAA et nous avons mis en évidence les facteurs de risque spécifiques de cette population. Ce constat a pu être établi grâce à la réalisation de la première méta-analyse sur le risque de décès par suicide après une TS, les méta-analyses antérieures ayant exploré le risque de décès après un PAA (80,87), et grâce à la réalisation d'une étude exhaustive sur le risque de décès par suicide après une TS.

Ensuite, nous avons utilisé des approches innovantes pour déterminer des sous-groupes de patients à risque de récidive de TS. Bien que les approches statistiques usuelles aient mis en évidence des facteurs de risque de récidive et de suicide chez les suicidants, le risque suicidaire doit se comprendre comme une interaction entre les facteurs de risque au cours de la vie. Nous avons donc utilisé des méthodes issues des sciences informatiques tel que les arbres de décision

pour mettre en évidence des sous-groupes de patients à risque. Nous avons également réalisé l'une des premières études pharmaco-épidémiologiques chez les suicidants qui a mis en évidence un risque de récidive plus important chez les patients qui consommaient des benzodiazépines et/ou des hypnotiques.

D'autre part, l'utilisation de grandes cohortes de patients suicidants est un atout majeur des travaux de cette thèse. En effet, nous avons analysé les cohortes ALGOS et Vigilans qui ont la même répartition des caractéristiques sociodémographiques et cliniques de la TS que les cohortes naturelles de suicidants. Soit, dans une cohorte naturelle de suicidants, la moyenne d'âge est aux alentours de 40 ans, avec une majorité de femmes, environ 80% à 90% sont des intoxications médicamenteuses volontaires et 5% des TS sont sévères qui nécessitent une hospitalisation en réanimation (55,56). L'utilisation de cohortes naturelles de suicidants est une force pour la généralisation des résultats à d'autres cohortes.

Enfin, à l'aide d'une méta-analyse, nous avons estimé le taux de mortalité par suicide dans l'année suivant une TS. Nous avons cependant démontré qu'il y avait peu d'études sur le sujet et une grande hétérogénéité entre les études ce qui peut biaiser la valeur estimée. Dans un second temps, une étude exhaustive de la mortalité dans une grande cohorte de suicidants a donc été effectuée. Dans cette analyse exhaustive, les causes de décès ont été recherchées auprès du médecin traitant ou du psychiatre prenant en charge le patient. Ce recueil auprès des médecins traitants, bien que plus couteux en temps, nous a semblé être un réel avantage par rapport à l'utilisation des registres nationaux de mortalité. En effet, les registres de mortalité nationaux tel que le registre français du CepiDC ont l'avantage de présenter les causes de mortalité de manière exhaustive sur un territoire donné. Toutefois, nous avons vu dans l'introduction qu'un grand nombre de décès était codé « de cause inconnue ». Or, il a été démontré que beaucoup de décès par suicide sont cachés derrière ces causes de décès inconnues (42,45,88). Les registres nationaux de mortalité ont donc tendance à sous-estimer le nombre de suicides. Une étude exhaustive des causes de décès chez les suicidants ne pouvait donc pas uniquement se baser sur ces données.

En deuxième lieu, notre travail de recherche comporte plusieurs points faibles. D'abord, nous avons retrouvé une grande proportion de données manquantes dans nos études. Ainsi, dans notre étude pharmaco-épidémiologique et dans l'évaluation de la formation Terra-Séguin, nous avons retrouvé environ 30% de données manquantes. Nous avons pris le parti d'imputer les données manquantes par la méthode des imputations multiples (89). Cette méthode robuste d'imputation permet, dans une certaine mesure, de limiter le biais lié aux données manquantes.

Ensuite, l'évaluation de la psychopathologie des suicidants n'a pas été appréhendée dans les cohortes Algos et Vigilans à l'inclusion. Dans l'étude Algos, une évaluation diagnostique courte avait été réalisée à l'inclusion et ne recherchait que le trouble lié à l'usage de l'alcool, la dépression, le trouble anxieux et l'anorexie mentale. Puis, une évaluation psychiatrique standardisée (la Mini International Neuropsychiatric Interview (MINI) (77)) était réalisée à 6 et 14 mois. L'absence d'évaluation du trouble psychopathologique dans le dispositif Vigilans ne permet pas d'analyser l'association entre le trouble psychiatrique et la récidive de TS ou le décès par suicide ni d'ajuster nos analyses sur le trouble présenté. De plus, le MINI réalisé dans l'étude Algos mettait en évidence un nombre élevé de patients présentant un trouble de l'usage d'alcool. Ce taux élevé de patients présentant un trouble de l'usage d'alcool est à mettre en lien avec le taux particulièrement élevé de ce trouble dans la région des Hauts-de-France (90). La prévalence élevée du trouble de l'usage d'alcool dans notre étude peut gêner la généralisation des résultats que nous avons obtenu à d'autres populations de suicidants.

Concernant l'étude pharmaco-épidémiologique de l'association des psychotropes avec la récidive de TS, plusieurs limites peuvent être soulevées. Alors que nous avons mis en évidence une association entre la consommation de benzodiazépines et/ou d'hypnotiques et le risque de récidive de TS plusieurs points méritent d'être discutés. D'abord, les informations obtenues sur la consommation de psychotropes étaient déclarées par le patient lors d'un entretien téléphonique à 6 mois après une TS ce qui expose à un biais de mémorisation. Ensuite, la dose de traitement prise par le patient, la durée pendant laquelle le traitement a été pris et la prise concomitante ou non des traitements n'était pas appréhendés dans cette analyse. Enfin, il n'a pas été possible d'analyser plus précisément l'effet de certaines sous-classes ou de certains psychotropes sur le risque de récidive. Cette étude exploratoire de l'impact des psychotropes sur la récidive de TS rapporte un sur-risque lié à certaines classes qui mérite d'être évalué par des travaux supplémentaires.

Enfin, la dernière limite de notre travail concerne l'évaluation de la formation d'agents sentinelles dans les maisons de retraite. En effet, afin d'évaluer l'efficacité de cette formation sur le nombre de TS et de suicide dans les maisons de retraite, dans l'idéal, un essai randomise et contrôlé aurait dû être réalisé. A l'aide de notre étude pilote, nous avons essayé de déterminer l'efficacité de la formation Terra Séguin sur la réduction du nombre de TS et de suicides dans les maisons de retraite. Néanmoins, l'apport d'arguments indirects sur l'efficacité de la formation est moins coûteux dans un premier temps et permet d'apporter des arguments pour la réalisation d'études ultérieures.

# V. PERSPECTIVES

Alors que nos travaux de recherche se sont appuyés sur les données des cohortes Algos et Vigilans, il parait intéressant de répliquer nos résultats sur des données nationales. En effet, nous avons démontré que des sous-groupes de patients étaient à risque de récidive et de décès par suicide dans nos cohortes avec des approches innovantes. Reproduire cette méthodologie sur une plus grande cohorte permettrait de confirmer ou d'infirmer nos résultats, afin d'accroître notre vigilance pour les patients à risque. De plus, l'utilisation de données nationales permettrait d'être plus précis dans nos analyses et notamment lorsqu'il s'agit du lien entre les psychotropes et la récidive de TS. L'enrichissement des bases de remboursement de la caisse nationale d'assurance maladie et l'amélioration de l'accessibilité au Système National des Données de Sante (SNDS) offrent des pistes intéressantes pour des futures études (91).

Les patients souffrant d'un trouble psychiatrique ont une diminution de leur espérance de vie. Alors que cette thèse était consacrée à la morbi-mortalité des suicidants, d'autres populations spécifiques à risque de suicide méritent d'être étudiés. En effet, les patients présentant un trouble de stress post-traumatique (TSPT) seraient également plus à risque d'avoir des comportements suicidaires (92,93). Il nous parait donc intéressant de déterminer dans quelle mesure le TSPT est associé au risque de récidive suicidaire chez les suicidants. Déterminer si la présence d'un antécédent de TSPT est associée à une augmentation du risque de récidive chez les suicidants, en ajustant nos analyses sur les autres troubles psychiatriques, est important pour progresser dans la prévention du suicide. Cette étude sera réalisée prochainement à l'aide de la cohorte ALGOS et fera l'objet d'une publication dans une revue internationale.

Enfin, bien que les suicidants soient particulièrement à risque de récidive et de décès par suicide, les patients souffrant de dépression constituent une autre population spécifique dont la mortalité est élevée (26,94). La morbi-mortalité des patients souffrant de dépression peut être étudiée en analysant leur parcours de soins à l'aide des données du SNDS. Nous avons pour projet d'évaluer la ré-hospitalisation, les motifs de ré-hospitalisation dont la tentative de suicide, les traitements consommés et la mortalité de ces patients. La mise en évidence de facteurs de risque de morbidité par TS et de mortalité chez ces patients est essentielle en psychiatrie étant donné la prévalence élevée de patients déprimés qui sont amenés à être pris en charge.

En conclusion, les patients souffrant d'un trouble psychiatrique ont une surmortalité élevée liée à des taux élevés de décès par suicide mais également à une surmortalité de pathologies non-psychiatriques telles que les maladies cardio-vasculaires et les cancers. Dans ce travail de thèse, nous avons analysé plus spécifiquement le devenir des patients ayant fait une TS. En effet, les suicidants sont particulièrement à risque de récidive et de décès prématuré. Nous avons tenté de mettre en évidence de nouveaux facteurs de risque de récidive par des méthodes originales et de déterminer les causes de décès prématuré ainsi que les facteurs de risque qui sont impliqués. La mise en évidence de groupes de patients à risque de récidive et de décès est importante si l'on souhaite affiner notre évaluation clinique et améliorer les dispositifs de prévention existants. Par ailleurs, l'évaluation des dispositifs de prévention a fait l'objet de la dernière partie de cette thèse à l'aide d'un exemple d'évaluation de la formation d'agents sentinelles. Notre travail offre des perspectives intéressantes avec l'élaboration de nouveaux projets sur d'autres populations spécifiques dont la morbi-mortalité par TS et suicide est élevée : les patients souffrant de dépression ou d'un trouble de stress post-traumatique. La mise en exergue des causes de morbidité et de mortalité par des études épidémiologiques et l'identification de facteurs de risque chez les patients souffrant de troubles psychiatriques permet d'améliorer à la fois la prise en charge psychiatrique mais également la prise en charge des comorbidités non psychiatriques de nos patients. Une prise en charge globale des patients est essentielle si l'on souhaite améliorer leur qualité de vie et réduire l'écart d'espérance de vie avec la population générale.

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