Managing Suicidal Ideation in a Breast Cancer Cohort Seeking Reconstructive Surgery

Tiffany N.S. Ballard, MD[1*]
Xiaoxue Chen, BS[1]
Hyungjin M. Kim, ScD[2,3]
Jennifer B. Hamill, MPH[1]
Andrea L. Pusic, MD, MHS[4]
Edwin G. Wilkins, MD, MS[1]
Randy S. Roth, PhD[5]

[1]Section of Plastic Surgery, [2]Center for Statistical Consultation and Research, [3]Department of Biostatistics, [5]Department of Physical Medicine and Rehabilitation,University of Michigan, Ann Arbor, MI

[4]Division of Plastic and Reconstructive Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY

*Corresponding Author:
1500 E. Medical Center Drive, 2130 Taubman Center, SPC 5340, Ann Arbor, MI 48109
Phone: 734-936-5895, Fax: 734-763-5354, tballard@med.umich.edu

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/pon.4017

Key Points:

- Published literature on suicidal ideation among women with breast cancer undergoing mastectomy and reconstruction is limited.
- Psychological distress was assessed in a cohort of over 1,900 women with breast cancer enrolled in a prospective, multicenter study focusing on reconstruction outcomes.
- Nearly one in six women reported moderate-to-severe levels of anxiety and depression.
- Fourteen women reported significant suicidal ideation, prompting the development of a response system to enable triage to appropriate mental health services.
- Future studies should consider implementing methods to identify high-risk patients in their cohort.

Introduction

Emotional and social adaptation is a central challenge for women with recently diagnosed breast cancer [1]. Prevalence rates for anxiety and depressive disorders among a heterogeneous sample of cancer patients are estimated to range from 10 to 40% [2,3], and women with newly diagnosed breast cancer demonstrate comparable rates of affective distress [4]. As a result, breast reconstruction outcome studies routinely assess psychological variables and their influence on various patient-specific outcomes such as aesthetic satisfaction and functional status. While these studies typically include measures of preoperative depression and anxiety as possible predictors of clinical outcomes, relatively little attention has been paid to the identification of suicidal ideation (SI) in this cohort. This may seem surprising given evidence that depression is highly prevalent among cancer patients and, when increasingly severe, presents a primary risk for SI and intention [5]. While numerous studies describe the incidence of suicide among cancer patients in general [6], and women with breast cancer more specifically [7], there is sparse information on the prevalence of suicidal ideation among these populations. The assessment of SI in breast cancer patients presenting for reconstruction is in line with the American College of Surgeons (ACS) Commission on Cancer guidelines for distress screening of all cancer patients by 2015 [8].

We examined the prevalence of preoperative anxiety and depression among women enrolled in an ongoing prospective study of post-mastectomy breast reconstruction procedure outcomes. The prevalence of moderate-to-severe SI challenged the study team to devise an identification and response system to intervene with potential at-risk patients and triage them to appropriate mental health attention. We describe this system and propose its consideration for future surgical outcome studies where depression and SI are of reasonable concern.

Methods

Study Population

Patients were recruited as part of the Mastectomy Reconstruction Outcomes Consortium Study, a five-year prospective, multicenter cohort study comparing long-term outcomes of common post-mastectomy breast reconstruction procedures. Eligible subjects included women ≥18 years undergoing first-time unilateral or bilateral breast reconstruction. Only women with breast cancer undergoing immediate reconstruction were included in this analysis. Appropriate approval from the Institutional Review Board (IRB) at each participating site was obtained.

Data Collection

Prior to surgery, patients completed a battery of patient-reported outcome questionnaires soliciting information regarding sociodemographic status, general well-being, treatment satisfaction, pain, and psychosocial status. All data are collected via Velos (Velos Inc., Fremont, CA), a web-based clinical trial management system. For the current study, we specifically analyzed preoperative data from two measures of anxiety and depressive symptoms.

Measures

Anxiety was evaluated by the Generalized Anxiety Disorder (GAD-7) scale [9], a seven-item self-report inventory that asks respondents to report the frequency of anxiety symptoms over the previous two weeks from "none" (0 score) to "daily" (score of 3). A patient's level of anxiety is scaled as none/minimal (0-4), mild (5-9), moderate (10-14), or severe (15-21). A GAD-7 score of ≥10 has a sensitivity of 89% and a specificity of 82% for a diagnosis of generalized anxiety disorder.

Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9) [7], a nine-item self-report inventory that quantifies the frequency of depressive symptoms over the previous two weeks. Depression levels are interpreted as none/minimal (0-4), mild (5-9), moderate (10-14), moderately severe (15-21), or severe (20-27). PHQ scores of ≥10 have a sensitivity of 88% and specificity of 88% for a diagnosis of major depression. Notably, the last item on the PHQ-9 asks patients to report the frequency of suicidal thoughts and has been found to be significantly associated with suicidality in cancer patients [11]. Significant SI for this study was defined as a score of 2 or 3 reflecting thoughts of suicide occurring more than half the days of the week or every day.

Results

Of a total subject pool of 2378, 2144 (90.2%) women had a diagnosis of breast cancer. Immediate post-mastectomy reconstruction was performed in 1922 (89.6%), with 54.9% undergoing bilateral procedures. The majority underwent implant-based reconstruction (71.6%) compared to autologous tissue (25.6%). Among the potential study sample, 1912 (99.5%) women completed the GAD-7 and 1921 (99.9%) completed the PHQ-9 preoperatively. The mean age of women completing the questionnaires was 49.4 ± 10.0 years.

A total of 337 (17.6%) patients reported moderate or severe anxiety, while 314 (16.3%) indicated moderate or severe depression. Of greatest concern, 14 (0.7%) patients reported significant SI. Two of these women reported daily thoughts of suicide.

Discussion

Our findings replicate previous investigations demonstrating relatively higher rates of anxiety and depressive symptoms among women with breast cancer [2]. Over 16% of our sample reported *moderate-to-severe* anxiety and depressive symptoms, suggesting that these patients suffered potentially clinically significant emotional distress. Assessing for psychological distress may be particularly relevant for the cohort of women seeking immediate reconstruction as they may manifest more acute and severe depressive symptoms when compared to women who choose mastectomy alone or delayed reconstruction [12].

The finding of greatest concern was that 14 patients reported suicidal thoughts more than half the days of the week, with two disclosing *daily* thoughts of suicide. However, the prevalence of SI in our cohort was low at 0.7% compared to a prior study using the PHQ-9 among a sample of cancer patients that found 7.8% of responders reporting significant SI [13]. Among the general population, SI prevalance ranges from 1-20% [14]. Obviously, the report of SI on a self-report survey is not a clinical determination of individual suicidal intention and risk, which requires a careful psychiatric inquiry based on known parameters of suicidality. Nonetheless, suicide risk is an important clinical concern for comprehensive cancer patient management, given its potential lethality and prevalence [5]. Several recent reports have raised concern for suicidality specifically among women with breast cancer or a history of breast surgery. For example, Riihimäki et al. observed that suicide was the second leading cause of non-cancer death among a cohort of women with a history of breast cancer [15]. Taken together, these preliminary findings suggest that while the rate of suicide among breast cancer patients remains quite low, suicidality should be a concern for all practitioners caring for this population [5].

Although our study is observational rather than interventional in nature, we recognized a responsibility to protect women deemed at risk based on their reported experience of frequent suicidal thoughts. Following IRB approval, a response system was developed to address the need for rapid assessment of patients with serious SI (Figure 1). The study's web-based data collection system, Velos, queries the database every 12 hours for newly-entered responses to question #9 on the PHQ-9 equivalent to significant suicidal thoughts (a score of 2 or 3). When such an entry is detected, an automatic email alert is sent to the study Principal Investigators (PIs), the site PI overseeing the study at the patient's treatment facility, and the MROC study manager. Upon receipt of the alert, the patient is contacted by a qualified member of her healthcare team to assess safety and provide psychological support. Although contact procedures vary by site, a clinician with a mental health background, such as an oncology nurse or social worker, in addition to the site PI, is usually identified to contact the patient. Each site has developed its own process to facilitate a referral to social work or psychiatry, either urgently or expediently, depending on the perceived severity of the suicide risk. It is ultimately the responsibility of the treatment site PI to ensure the patient is contacted. Since the system is automatic, it is in operation 24 hours a day. Most importantly, it effectively enables the study team to intervene in a timely fashion when patients report frequent suicidal thoughts. To date, the majority of patients have been contacted within 24 hours, with delays most often a result of patients traveling out of town or not answering their telephone.

Health care practitioners frequently fail to recognize distress in the cancer patient population [5]. It is likely that reconstruction outcome studies involving breast cancer patients, even those that obtain preoperative patient distress measures, are similarly unaware of clinically significant distress among enrolled subjects. In these studies, baseline psychological measures are typically relegated to a data bank and become operative only once statistical analysis is undertaken to

evaluate surgical outcomes. As a result, relevant clinical information that could be potentially crucial for intervening with appropriate mental health services is obscured. While it is unrealistic to expect surgeons to become experts in suicide assessment and intervention, our study illustrates how an automated identification and triage system can be established to address psychological morbidity in cancer patients seeking surgical intervention.

In conclusion, our findings support the new standards of the ACS Commission on Cancer requiring distress screening for all new cancer patients. The baseline questionnaires identified women who were troubled by recurrent and strong SI, which prompted the development of a response system to address these patients' needs for expedited psychiatric intervention. Not only do our results demonstrate that approximately one-in-six breast cancer patients seeking reconstruction report moderate-to-high levels of distress, but that an automated response system can effectively alert study members about high-risk patients who require urgent mental health services.

Acknowledgement
The study was supported by grants from the Plastic Surgery Foundation and National Cancer Institute (1R01CA152192).

References

1. Kadan-Lottick NS, Vanderwerker LC, Block SD, et al. Psychiatric disorders and mental health services use in patients with advanced cancer: A report from the Coping with Cancer Study. *Cancer* 2005;**104**:2872-2881. DOI:10.1002/cncr.21532.
2. Britzenhofe-Szoc KM, Tomer TL, Li Y, Kissane DW, Zabora JR. Mixed anxiety/depression symptoms in a large cancer cohort: Prevalence by cancer type. *Psychosomatics* 2009; **50**:383-391. DOI: 10.1176/appi.psy.50.4.383.
3. Massie MJ. Prevalence of depression in patients with cancer. *Journal of the National Cancer Institute Monographs* 2004; **32**:57-71. DOI: 10.1093/jncimonographs/lgh014.
4. Khan F, Amatya B, Pallant JF, Rajapaksa I. Factors associated with long-term functional outcomes and psychological sequelae in women after breast cancer. *Breast* 2012;**21**: 314-320. DOI:10.1016/j.breast.2012.01.013.
5. Die Trill M. Psychological aspects of depression in cancer patients: An update. *Annals of Oncology* 2012; **23**(Suppl 10):302-305. DOI:10.1093/annonc/mds350.
6. Anguiano L, Mayer DK, Piven ML, Rosenstein D. A literature review of suicide in cancer patients. *Cancer Nursing* 2012;**35**:E14-E26. DOI: 10.1097/NCC.0b013e31822fc76c.
7. Güth U , Myrick ME, Reisch T, et al. Suicide in breast cancer patients: An individual-centered approach provides insight beyond epidemiology. *Acta Oncologica* 2011;**50**:1037-1044. DOI:10.3109/0284186X.2011.602112.
8. Cancer program standards 2012, Version 1.2: Ensuring patient-centered care [*American College of Surgeons Commission on Cancer* web site]. 2012. Available at: http://www.facs.org/cancer/coc/programstandards2012.html. Accessed January 9, 2014.
9. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine* 2006;**166**:1092-1097. DOI:10.1001/archinte.166.10.1092.
10. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine* 2001;**16**:606-613. DOI:10.1046/j.1525-1497.2001.016009606.x.
11. Walker J, Hansen C, Hodges L, et al. Screening for suicidality in cancer patients using Item 9 of the nine-item patient health questionnaire: Does the item score predict who requires further assessment? *General Hospital Psychiatry* 2010;**32**:218-220. DOI:10.1016/j.genhosppsych.2009.11.011.
12. Roth RS, Lowery JC, Davis J, Wilkins EG. Quality of life and affective distress in women seeking immediate versus delayed breast reconstruction after mastectomy for breast cancer. *Plastic Reconstructive Surgery* 2005;**116**:993-1002. DOI:10.1097/01.prs.0000178395.19992.ca.
13. Walker J, Waters RA, Murray G, Swanson H et al. Better off dead: Suicidal thoughts in cancer patients. *Journal of Clinical Oncology* 2008;**26**:4725-4730. DOI: 10.1200/JCO.2007.11.8844.

14. Casey P, Dunn G, Kelly B *et al.* The prevalence of suicidal ideation in the general population: Results from the Outcome of Depression International Network (ODIN) study. *Social Psychiatry and Psychiatric Epidemiology* 2008;**43**:299–304. DOI: 10.1007/s00127-008-0313-5.
15. Riihimäki M, Thomsen H, Brandt A, et al. Death causes in breast cancer patients. *Annals of Oncology* 2012;**23**:604-610. DOI:10.1093/annonc/mdr160.

Figure 1. Response system developed to identify and contact at-risk patients.
PI, principal investigator.

COPYRIGHT TRANSFER AGREEMENT

WILEY-BLACKWELL

Date: 02/10/15 Contributor name: Tiffany W. S. Ballard, MD

Contributor address: 1500 E. Medical Center Dr., 2130 Taubman Center, SPC 5340 Ann Arbor, MI 48109

Manuscript number (if known): _____

Re: Manuscript entitled Managing Suicidal Ideation in a Breast Cancer Cohort Seeking Reconstructive Surgery (the "Contribution")

for publication in Psycho-Oncology (the "Journal")

published by Wiley-Blackwell ("Wiley-Blackwell").

Dear Contributor(s):
Thank you for submitting your Contribution for publication. In order to expedite the editing and publishing process and enable Wiley-Blackwell to disseminate your Contribution to the fullest extent, we need to have this Copyright Transfer Agreement signed and returned as directed in the Journal's instructions for authors as soon as possible. If the Contribution is not accepted for publication, or if the Contribution is subsequently rejected, this Agreement shall be null and void. **Publication cannot proceed without a signed copy of this Agreement.**

A. COPYRIGHT

1. The Contributor assigns to Wiley-Blackwell, during the full term of copyright and any extensions or renewals, all copyright in and to the Contribution, and all rights therein, including but not limited to the right to publish, republish, transmit, sell, distribute and otherwise use the Contribution in whole or in part in electronic and print editions of the Journal and in derivative works throughout the world, in all languages and in all media of expression now known or later developed, and to license or permit others to do so.

2. Reproduction, posting, transmission or other distribution or use of the final Contribution in whole or in part in any medium by the Contributor as permitted by this Agreement requires a citation to the Journal and an appropriate credit to Wiley-Blackwell as Publisher, and/or the Society if applicable, suitable in form and content as follows: (Title of Article, Author, Journal Title and Volume/Issue, Copyright © [year], copyright owner as specified in the Journal). Links to the final article on Wiley-Blackwell's website are encouraged where appropriate.

B. RETAINED RIGHTS

Notwithstanding the above, the Contributor or, if applicable, the Contributor's Employer, retains all proprietary rights other than copyright, such as patent rights, in any process, procedure or article of manufacture described in the Contribution.

C. PERMITTED USES BY CONTRIBUTOR

1. Submitted Version. Wiley-Blackwell licenses back the following rights to the Contributor in the version of the Contribution as originally submitted for publication:

a. After publication of the final article, the right to self-archive on the Contributor's personal website or in the Contributor's institution's/employer's institutional repository or archive. This right extends to both intranets and the Internet. The Contributor may not update the submission version or replace it with the published Contribution. The version posted must contain a legend as follows: This is the pre-peer reviewed version of the following article: FULL CITE, which has been published in final form at [Link to final article].

b. The right to transmit, print and share copies with colleagues.

2. Accepted Version. Re-use of the accepted and peer-reviewed (but not final) version of the Contribution shall be by separate agreement with Wiley-Blackwell. Wiley-Blackwell has agreements with certain funding agencies governing reuse of this version. The details of those relationships, and other offerings allowing open web use, are set forth at the following website: http://www.wiley.com/go/funderstatement. NIH grantees should check the box at the bottom of this document.

3. Final Published Version. Wiley-Blackwell hereby licenses back to the Contributor the following rights with respect to the final published version of the Contribution:

a. Copies for colleagues. The personal right of the Contributor only to send or transmit individual copies of the final published version in any format to colleagues upon their specific request provided no fee is charged, and further-provided that there is no systematic distribution of the Contribution, e.g. posting on a listserve, website or automated delivery.

b. Re-use in other publications. The right to re-use the final Contribution or parts thereof for any publication authored or edited by the Contributor (excluding journal articles) where such re-used material constitutes less than half of the total material in such publication. In such case, any modifications should be accurately noted.

c. Teaching duties. The right to include the Contribution in teaching or training duties at the Contributor's institution/place of employment including in course packs, e-reserves, presentation at professional conferences, in-house training, or distance learning. The Contribution may not be used in seminars outside of normal teaching obligations (e.g. commercial seminars). Electronic posting of the final published version in connection with teaching/training at the Contributor's institution/place of employment is permitted subject to the implementation of reasonable access control mechanisms, such as user name and password. Posting the final published version on the open Internet is not permitted.

d. Oral presentations. The right to make oral presentations based on the Contribution.

4. Article Abstracts, Figures, Tables, Data Sets, Artwork and Selected Text (up to 250 words).

a. Contributors may re-use unmodified abstracts for any non-commercial purpose. For on-line uses of the abstracts, Wiley-Blackwell encourages but does not require linking back to the final published versions.

b. Contributors may re-use figures, tables, data sets, artwork, and selected text up to 250 words from their Contributions, provided the following conditions are met:

(i) Full and accurate credit must be given to the Contribution.
(ii) Modifications to the figures, tables and data must be noted. Otherwise, no changes may be made.
(iii) The reuse may not be made for direct commercial purposes, or for financial consideration to the Contributor.
(iv) Nothing herein shall permit dual publication in violation of journal ethical practices.

D. CONTRIBUTIONS OWNED BY EMPLOYER

1. If the Contribution was written by the Contributor in the course of the Contributor's employment (as a "work-made-for-hire" in the course of employment), the Contribution is owned by the company/employer which must sign this Agreement (in addition to the Contributor's signature) in the space provided below. In such case, the company/employer hereby assigns to Wiley-Blackwell, during the full term of copyright, all copyright in and to the Contribution for the full term of copyright throughout the world as specified in paragraph A above.

2. In addition to the rights specified as retained in paragraph B above and the rights granted back to the Contributor pursuant to paragraph C above, Wiley-Blackwell hereby grants back, without charge, to such company/employer, its subsidiaries and divisions, the right to make copies of and distribute the final published Contribution internally in print format or electronically on the Company's internal network. Copies so used may not be resold or distributed externally. However the company/employer may include information and text from the Contribution as part of an information package included with software or other products offered for sale or license or included in patent applications. Posting of the final published Contribution by the institution on a public access website may only be done with Wiley-Blackwell's written permission, and payment of any applicable fee(s). Also, upon payment of Wiley-Blackwell's reprint fee, the institution may distribute print copies of the published Contribution externally.

E. GOVERNMENT CONTRACTS

In the case of a Contribution prepared under U.S. Government contract or grant, the U.S. Government may reproduce, without charge, all or portions of the Contribution and may authorize others to do so, for official U.S. Government purposes only, if the U.S. Government contract or grant so requires. (U.S. Government, U.K. Government, and other government employees: see notes at end)

F. COPYRIGHT NOTICE

The Contributor and the company/employer agree that any and all copies of the final published version of the Contribution or any part thereof distributed or posted by them in print or electronic format as permitted herein will include the notice of copyright as stipulated in the Journal and a full citation to the Journal as published by Wiley-Blackwell.

G. CONTRIBUTOR'S REPRESENTATIONS

The Contributor represents that the Contribution is the Contributor's original work, all individuals identified as Contributors actually contributed to the Contribution, and all individuals who contributed are included. If the Contribution was prepared jointly, the Contributor agrees to inform the co-Contributors of the terms of this Agreement and to obtain their signature to this Agreement or their written permission to sign on their behalf. The Contribution is submitted only to this Journal and has not been published before. (If excerpts from copyrighted works owned by third parties are included, the Contributor will obtain written permission from the copyright owners for all uses as set forth in Wiley-Blackwell's permissions form or in the Journal's Instructions for Contributors, and show credit to the sources in the Contribution.) The Contributor also warrants that the Contribution contains no libelous or unlawful statements, does not infringe upon the rights (including without limitation the copyright, patent or trademark rights) or the privacy of others, or contain material or instructions that might cause harm or injury.

CHECK ONE BOX:

☑ Contributor-owned work

ATTACH ADDITIONAL SIGNATURE PAGES AS NECESSARY

Contributor's signature Tiffany N.S. Ballard, MD Date 02/10/15

Type or print name and title Tiffany N.S. Ballard, MD Resident, Plastic Surgery

Co-contributor's signature Date

Type or print name and title

☐ Company/Institution-owned work (made-for-hire in the course of employment)

Company or Institution (Employer-for-Hire) Date

Authorized signature of Employer Date

☐ U.S. Government work

Note to U.S. Government Employees
A contribution prepared by a U.S. federal government employee as part of the employee's official duties, or which is an official U.S. Government publication, is called a "U.S. Government work," and is in the public domain in the United States. In such case, the employee may cross out Paragraph A.1 but must sign (in the Contributor's signature line) and return this Agreement. If the Contribution was not prepared as part of the employee's duties or is not an official U.S. Government publication, it is not a U.S. Government work.

☐ U.K. Government work (Crown Copyright)

Note to U.K. Government Employees
The rights in a Contribution prepared by an employee of a U.K. government department, agency or other Crown body as part of his/her official duties, or which is an official government publication, belong to the Crown. U.K. government authors should submit a signed declaration form together with this Agreement. The form can be obtained via http://www.opsi.gov.uk/advice/crown-copyright/copyright-guidance/publication-of-articles-written-by-ministers-and-civil-servants.htm

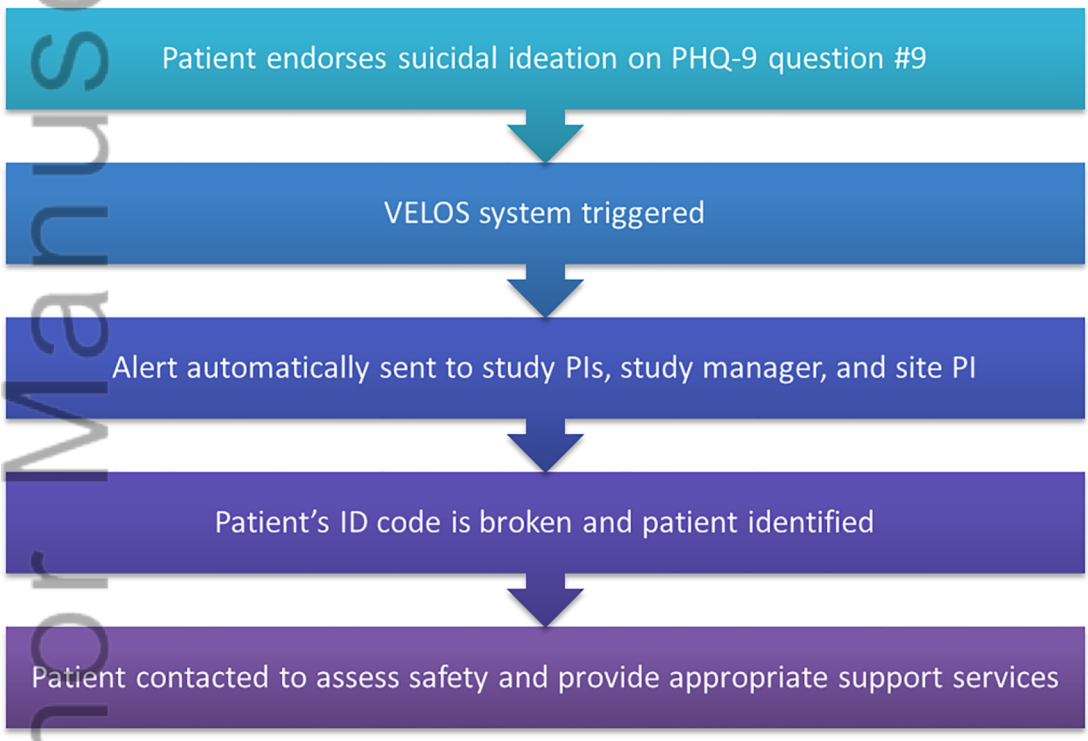
☐ Other Government work

Note to Non-U.S., Non-U.K. Government Employees
If your status as a government employee legally prevents you from signing this Agreement, please contact the editorial office.

☐ NIH Grantees

Note to NIH Grantees
Pursuant to NIH mandate, Wiley-Blackwell will post the accepted version of Contributions authored by NIH grant-holders to PubMed Central upon acceptance. This accepted version will be made publicly available 12 months after publication. For further information, see www.wiley.com/go/nihmandate.

CTA-A



PON_4017_F1.tif