Letters to the Editor

Reassessing Mental Health Treatment Utilization Reduction in Transgender Individuals After Gender-Affirming Surgeries: A Comment by the Editor on the Process

On October 4, 2019, we published an article by Bränström and Pachankis in which it was reported that observed reductions in mental health treatment utilization lent support to the decision to provide gender-affirming surgeries to those who seek them (1). After this article’s publication, we received several letters calling into question the statistical analyses employed and the conclusions drawn from said analyses. These letters follow this comment (2–8).

We enlisted the services of a statistical reviewer to look again at the article as well as the letters we received. We then sent the letters we received and the results of this statistical review, which called for a matched-pairs analysis, to the original authors. The study authors complied with the request to perform an additional analysis, as presented in their letter response (9).

We sent the original letters, statistical review, and author response to a second statistical reviewer. The response from this consultation convinced us that, given that the study used neither a prospective cohort design nor a randomized controlled trial design, the conclusion that “the longitudinal association between gender-affirming surgery and reduced likelihood of mental health treatment lends support to the decision to provide gender-affirming surgeries to transgender individuals who seek them” was too strong. In the August 2020 issue of the Journal, we are publishing a correction to this effect and including an addendum to the article pointing to this postpublication discussion and process, both of which were composed with contributions and approval from the original article authors.

We thank the letter writers, statistical reviewers, and the original study authors—as well as the editorialist we invited to place this study’s findings in context (10)—for helping us to make clear to our readers and for the literature what the article shows and what still remains to be investigated in future research.

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Ned H. Kalin, M.D.
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Methodological Shortcomings Undercut Statement in Support of Gender-Affirming Surgery

TO THE EDITOR: The article by Bränström and Pachankis (1) has the stated aim “to ascertain the prevalence of mood and anxiety disorder health care visits and antidepressant and anxiolytic prescriptions in 2015 as a function of gender incongruence diagnosis and gender-affirming hormone and surgical treatment in the entire Swedish population.” The authors conclude that “the longitudinal association between gender-affirming surgery and reduced likelihood of mental health treatment lends support to the decision to provide gender-affirming surgeries to transgender individuals who seek them.” In support of this claim, the authors report that the time since “last gender-affirming surgery” (in 2005–2014) was associated with reduced “mental health treatment” (a combined variable of outpatient visits with a diagnosis of a mood or anxiety disorder and/or prescriptions for antidepressants or anxiolytics) during 2015 (adjusted odds ratio = 0.92, 95% CI = 0.87–0.98). The authors have also

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shown that the group of people diagnosed with gender incongruence have a dramatically worse overall mental health outcome than the general population, which is, in fact, the answer to their stated aim and research question, but this finding is not even referred to in the title or in the Conclusions section of the article.

In view of the claim that surgery was shown to be an efficient treatment for gender incongruence, the following issues have to be raised:

1. Variables, hypotheses, and analytical strategies were not described pre hoc. Adequate power analyses and corrections for multiple comparisons were not provided.

2. The article is vague or noninformative with respect to key aspects. Biological sex ratios are not provided. Surgeries for complications or even unrelated surgeries (e.g., in the skin or the larynx) may have been included. Lithium and atypical antipsychotic medications were not included as treatments for mood disorders, while a histamine blocker such as hydroxyzine, which is mainly used for non-mental health problems, was. Outpatient visits for mood and anxiety disorders were included as “mental health treatment” but not for sleeping disorders, substance-related disorders, major mental disorders, or any inpatient psychiatric treatment.

3. The nonnormal distribution of data, known secular changes, age effects, or people who left Sweden and moved abroad, died from suicide or other causes, or had surgery to desist were not considered in the interpretation of the analyses.

As the article stands, we actually have no way of knowing whether the four reported analyses of purported treatment effects (time elapsed since start of hormones OR since last surgery BY outpatient mental health treatment OR suicide attempt–related hospitalization), one of which was statistically significant by a small margin, were the first analyses made or the final setup chosen for publication after a “fishing expedition” in the database.

These methodological shortcomings preclude any statement on the suitability of early surgery in persons seeking treatment for gender noncongruence based on the results presented in this article.

REFERENCE


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Gender-Affirmation Surgery Conclusion Lacks Evidence

TO THE EDITOR: We have concerns regarding severe shortcomings in the study by Bränström and Pachankis (1) that call into question the authors’ conclusion that it “provides timely support for policies that ensure coverage of gender-affirming treatments.”

This study covered outcomes only for calendar year 2015 for all individuals living in Sweden on December 31, 2014. The retrospective metric of “time since last gender-affirming surgery” in Figure 1 in the article is easily misinterpreted as a prospective 10-year follow-up that did not occur and leaves open the question of number and type of prior surgeries.

The 2,679 individuals diagnosed with gender incongruence in Sweden is a full order of magnitude below prevalence expectations from DSM-5. Table 3 in the article indicates that 38% of these individuals had any kind of gender-affirming surgery, but only 53% of those had surgery of reproductive organs. Given that such treatment in Sweden is free, ample loss to follow-up is implied.

Measured outcomes were limited to “mood and anxiety disorder health care visits, antidepressant and anxiolytic prescriptions, and hospitalization after a suicide attempt.” This selection excludes completed suicides, suicide attempts without subsequent hospitalization, health care visits and hospitalizations for other medical or psychological issues still related to gender-affirming surgeries, individuals refusing treatment, and individuals choosing self-medication with alcohol or illicit substances. Again, significant loss to follow-up must be considered before declaring success.

Dhejne’s cohort study of 324 persons in Sweden undergoing sex-reassignment surgery used 30 years of data, population controls, and matching by birth year, birth sex, and reassigned sex (2). Through the Hospital Discharge Register, the authors evaluated discharge diagnoses, external causes of morbidity and mortality, and surgical procedure codes. Compared with the general population, patients who had sex reassignment surgery had 19 times the rate of completed suicide, almost three times the rate of all-cause mortality, nearly three times the rate of inpatient psychiatric care, and close to five times the rate of suicide attempts.

These important findings could have been updated to the current period, given the sharp rise in adolescent case presentations, use of puberty blockers, and changes in cross-sex hormones from agents like ethinyl estradiol to 17β-estradiol.

For those whose last surgery was 10 or more years earlier, how many completed suicide, died of other causes, or left Sweden prior to study initiation? A drop in hospitalizations for suicide attempts alone provides a very incomplete picture. When the data for such findings are accessible in the Swedish national registers, this omission is glaring.

The lack of control subjects, the limited 1-year time frame, and the avoidance of examining completed suicides and psychiatric hospitalizations are substantial study shortfalls.
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The study supports only weak conclusions about psychiatric medication usage and nothing decisive about suicidality. In overlooking so much available data, this study lacks the evidence to support its progender-affirmation surgery conclusion.

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Study of Transgender Patients: Conclusions Are Not Supported by Findings

TO THE EDITOR: The study of transgender individuals by Bränström and Pachankis claims to demonstrate a reduction in mental health treatment utilization after gender-affirming surgery but, in fact, demonstrates no such thing (1).

The only result they present that they claim is statistically significant is that there is an association between years since last gender-affirming surgery and recent mental health treatment (adjusted odds ratio = 0.92, 95% CI = 0.87–0.98). This result makes no sense as it stands because analysis of a quantitative measure against an outcome does not produce an odds ratio. Presumably, the authors must mean that each year since surgery is associated with an odds ratio of 0.92. There are also discrepancies between the data discussed in the text and in the tables. For example, the authors quote the percentage of patients with gender incongruence who received no treatment as 29% in the text but 29.6% in Table 3 and, more importantly, the percentage of patients who received surgery as 48% in the text but only 38.0% in the table. However, the key statistical criticism is that they have failed to carry out standard corrections for multiple testing. As they tested two interventions, hormone treatment and surgery, against two outcomes, mental health treatment and suicide attempts, they performed four tests. Because the upper confidence interval that they quote is very close to 1, it is obvious that if appropriate correction for multiple testing had been applied, then none of the results would have been deemed significant.

When one views the data on which these analyses are based, as presented in Figure 1 in the article, some very clear features emerge. First, there is obviously no general correlation between the outcomes and time since surgery. Rather, a spike in suicide attempts is seen in the year after surgery (in 2.8% of the patients), which falls off over the next 1–2 years, and to a lesser extent, there is also a spike in the proportion of patients receiving mental health treatment in the first year, going up to 45.3%. There is also a low rate of mental health treatment among patients who received surgery 10 or more years earlier. This may reflect the fact that in the past, patients with mental health problems would have been less likely to be offered surgery.

The study confirms the strong association between psychiatric morbidity and the experience of incongruity between gender identity and biological sex. However, the study does not demonstrate that either hormonal treatment or surgery has any effect on this morbidity. It seems that the main message of this article is that the incidence of mental health problems and suicide attempts is especially high in the year after the completion of gender-affirming surgery and that increased support in this period might be indicated.

REFERENCE


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Calling Into Question Whether Gender-Affirming Surgery Relieves Psychological Distress

TO THE EDITOR: The study by Bränström and Pachankis (1) shows a reduction in mental health treatments and hospitalization after suicide attempts with increased time after masculinizing or feminizing surgeries.

The data presented in Figure 1 in the article support findings from previous studies showing that transgender individuals have baseline mental health distress that is higher than that of the general population, but it is not possible to conclude from these data whether gender-affirming surgery relieves that distress.

According to the study, mental health utilization rates were highest in the perioperative period. However, the data also could be interpreted as showing that masculinizing or feminizing surgeries were the actual cause of increased mental health utilization. Surgery is a known risk factor for the development of depression (2) and may have caused a
deterioration in mental health in a population of individuals who already had more psychological distress, which abated with time since surgery. It is just as possible that mental health improved as individuals had fewer surgeries.

After the initial 1% drop in mental health visits in the first year after surgery, there was very little change in mental health visits (5.6% over 9 years), and there was a further 1% fall in the ≥10-year group. It is not clear what caused the reduction in the two markers for mental health distress past the 10-year mark. Loss to follow-up, death from suicide of the most psychologically distressed individuals, or death from cardiovascular disease, all known to be increased in the transgender population, could have falsely skewed the ≥10-year data. Comparisons with a control group would be best to answer these questions.

In addition, there are only 19 people in the ≥10-year group who underwent gender-affirming surgery. A total of 21.1% of them received mental health treatment, which is only four people. This means that a single mental health utilization event in either direction would change the calculated rate of utilization by 5%. However, the assertion that gender-affirming surgeries reduce mental health visits by 8% is highly dependent upon this sudden drop in rates in the ≥10-year group of only 19 people.

Finally, no information is given about the composition of the year 1 group and ≥10-year groups, but given the changing epidemiology of gender dysphoria in Sweden (3), the year 1 group likely included a higher percentage of younger natal females than the ≥10-year group, which likely had more older natal males, making comparisons between the year 1 and ≥10-year groups problematic.

Because of the limitations in the study design, it is not possible to determine the cause of the differences in mental health service utilization or whether true reductions in psychological distress actually occurred. Therefore, the authors’ conclusion that the results of their study should be interpreted to support policies that provide gender-affirming surgeries cannot be supported.

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The Effect of Gender-Affirming Treatment on Psychiatric Morbidity Is Still Undecided

TO THE EDITOR: In this issue of the Journal, Bränström and Pachankis study mental health treatment and suicide attempts in persons diagnosed with gender dysphoria in Sweden (1). Their claim that the study shows that gender-affirming treatment reduces the risk of mental health treatment and suicide attempts is misleading because the study design is flawed.

The authors first found what was already known (2): the rate of psychiatric morbidity is much higher in persons with gender dysphoria compared with the general population. The authors then explored if the risk for mental health treatment changes as a function of years since starting hormonal treatment. They find no effect (odds ratio=1.0), but they do find a trend toward increased risk of suicide attempts as a function of years since starting hormonal treatment. In their key analysis, allegedly showing that gender-affirming surgery decreases risk for psychiatric treatment and suicide attempts, they relate these negative outcomes to the number of years since surgery. Contrary to what the authors repeatedly claim, they do not employ a longitudinal design but conduct a retrospective analysis unfit for their research question.

First, the authors include only persons who were alive in 2014. That means that those who died by suicide before 2014—and hence were at highest risk for suicide attempt—are excluded and confound the results. Second, any analysis starting with a negative event is bound to find a decreased risk for related negative outcomes with increasing time after the event. To exemplify this point, the rate of antidepressant treatment would decrease with time after a suicide attempt. This does not mean that suicide attempts cause a decrease in risk of antidepressant treatment; it is merely a case of regression toward the mean. Third, persons undergoing gender transition have, by definition, contact with mental health services in Sweden. After the transition, persons are followed up by endocrinologists and sometimes general practitioners; only those with persistent mental health issues are followed in psychiatric care. The authors’ finding of lower rates of mental health treatment with increasing time after surgery is therefore not only a case of regression toward the mean, but it also follows from the standards of care and is not a proxy for improved mental health.

Because the authors do not present data prior to gender-affirming surgery, the study is uninformative with regard to the effects on psychiatric morbidity. Moreover, the authors miss the one conclusion that can be drawn: that the perioperative transition period seems to be associated with high risk for suicide attempt. Future research should use properly designed observational studies to answer the important question as to whether gender-affirming treatment affects psychiatric outcomes.

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The time elapsed since last surgical operation (of individuals with gender dysphoria, grouped according to gender dysphoria who were hospitalized for suicide attempt in 2015 for a suicide attempt. The authors do not state how many had not. There were 22 individuals who were hospitalized in 2015. The results confirm what is already known, that is, that as a group, persons with gender dysphoria suffer from poorer psychiatric health than the general population.

However, the title of the article implies that gender-correction surgery promotes mental health in this group, and the authors conclude in the Abstract section that the study “lends support to the decision to provide gender-affirming surgeries to transgender individuals who seek them.” In my opinion, this conclusion is not supported by the data presented in the article.

The most straightforward method to test whether surgery contributes to better psychological health would be to compare the health of those who underwent surgery with those who did not.

The authors noted that the last surgical correction was made (0.9% of 221) and one case 2–3 years after the last surgical treatment (0.5% of 198), while none occurred more than 3 years after the last surgery. Thus, 13 individuals (10 plus two plus one) of the 22 persons who were hospitalized for a suicide attempt in 2015 had undergone gender-correction surgery. Consequently, nine of them (22 minus 13) had not undergone any gender-affirmation surgery.

This corresponds to an odds ratio of 2.37 (95% CI 1.01–5.56, p=0.047). Hence, among the individuals examined in the study, the risk of being hospitalized for a suicide attempt was 2.4 times higher if they had undergone gender-correction surgery than if they had not. Whether this is a causal relation (i.e., that surgery actually worsens the poor mental health in individuals with gender dysphoria) cannot be determined. Nevertheless, the data presented in the article do not support the conclusion that surgery is beneficial to mental health in individuals with gender dysphoria.

TO THE EDITOR: The article by Bränström and Pachankis (1) examines the psychiatric health of persons who have obtained a diagnosis of gender dysphoria between 2005 and 2015 compared with the general population. The variables examined were psychiatric diagnosis, prescription of psychiatric drugs (anxiolytics and antidepressants), and hospitalization for suicide attempt in 2015.

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The persons diagnosed with gender dysphoria presented in the article, 1,018 had undergone surgery, while 1,661 had not. There were 22 individuals who were hospitalized in 2015 for a suicide attempt. The authors do not state how many of these individuals had received surgery, but this may be calculated by combining the data from Table 3 and Figure 1 in the article. Figure 1 shows the proportion of persons with gender dysphoria who were hospitalized for suicide attempt in 2015, grouped according to the time that had elapsed since the last gender-correction surgery. Table 3 shows the number of individuals with gender dysphoria, grouped according to the time elapsed since last surgical operation (“Time since last gender-affirming surgical treatment”).

By combining these data, we can calculate that 10 of the suicide attempts (2.8% of 353) occurred during the same year that the last surgical correction was made (“perioperative” group in Figure 1). Two cases occurred 1 year after the last surgical correction (0.9% of 221) and one case 2–3 years after the last surgical treatment (0.5% of 198), while none occurred more than 3 years after the last surgery. Thus, 13 individuals (10 plus two plus one) of the 22 persons who were hospitalized for a suicide attempt in 2015 had undergone gender-correction surgery. Consequently, nine of them (22 minus 13) had not undergone any gender-affirmation surgery.

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issues than those whose surgery happened longer ago, we would expect the decline in mental health treatment to be pronounced (see the solid line in Figure 2). The qualitative approximation of this curve with the reduction described by Bränström and Pachankis (in their Figure 1) is striking. Therefore, accounting for the increase in mental health issues from 2005, together with an assumption of increased mental health treatment due to this surgery, fits the data in the article and overturns the authors’ conclusions, suggesting that sex reassignment surgery is in fact associated with increased mental health treatment.

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