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Trajectories of gender expansive behavior in children and adolescents: a time-to-event analysis in a large health system-based cohort

By

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Master of Public Health

Epidemiology

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Abstract

Trajectories of gender expansive behavior in children and adolescents: a time-to-event analysis in a large health system-based cohort

By Stephanie B. Wagner

Objectives: Health care needs of transgender and gender diverse (TGD) children and adolescents is an increasingly important, but understudied, issue. Few studies have examined the likelihood of gender expansive behavior progressing to a TGD-specific diagnosis or gender affirming hormonal treatment (GAHT). This study aims to explore this using data from three geographically and demographically diverse integrated health care systems.
Methods: Electronic Health Records from 2006 to 2014 were used to ascertain study participants at Kaiser Permanente sites in Georgia, Northern California, and Southern California. Individuals were designated as having TGD status based on free-text keywords in clinical notes. Of 1,347 participants first presenting as TGD at age 3-17 years, 958 were enrolled without a TGD diagnosis and included in this analysis. Participants were followed until the event of interest (diagnostic code or first ordered GAHT prescription, analysis dependent), disenrollment from the health plan, or end of study follow-up (December 2014). Multivariable Cox proportional hazard models were used to compare incidence rates of events of interest across demographic groups with results expressed as hazard ratios (HR) and 95% confidence intervals (CI).
Results: Overall, 29% of participants received a TGD diagnosis and 25% were prescribed GAHT during follow-up. Approximately one quarter (24%) of TGD youth with male sex recorded at birth received a TGD diagnosis compared to one third (33%) of TGD youth who were recorded as female at birth (adjusted HR=1.3; 95% CI: 1.0, 1.7). TGD diagnosis was more common among those 15+ years at presentation when compared to those age 10-14 years and age 3-9 years (37% vs. 28% vs. 16%, respectively). Using the youngest group as reference, the adjusted HRs (95% CI) were 2.0 (1.3-3.0) for age 10-14 years and 2.7 (1.8-3.9) for age 15+ years. Racial/ethnic minorities were less likely to receive a diagnosis (26% vs. 33%) or be prescribed GAHT (21% vs. 29%) than their non-Hispanic white counterparts.
Conclusions: Rates of TGD-specific diagnosis and GAHT initiation in TGD youth differ significantly by age, sex recorded at birth, and race/ethnicity. These results have implications for future studies aimed at informing care of children with gender expansive behaviors.

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Introduction

Understanding the natural history of gender expansive behavior is an increasingly important issue in caring for transgender and gender diverse (TGD) children and adolescents. Changing definitions, evolving theories of gender identity development and availability of new data affect current understanding of the optimal care required to support TGD youth.

Gender identity is defined as the internal identification of where an individual falls on a range from maleness to femaleness, while TGD individuals are those whose gender identity does not fully match their recorded gender at birth (1). "Gender variant behavior" is a related term that describes behaviors that contrast with what society may term as "typical" or "sex-typed" (1). The language pertaining to individuals who experience distress with their assigned sex has changed in recent decades, particularly with the introduction of the term "gender dysphoria" in the Diagnostic and Statistical Manual of Mental Disorders (DSM) V to emphasize distress secondary to TGD identity rather than pathologizing TGD identity itself (1-4).

Currently there is controversy over when to start gender affirming therapies, particularly in a setting where we do not fully understand the natural history of gender expansive behaviors. Guidelines issues by the Endocrine Society and the World Professional Association for Transgender Health (WPATH) recommend psychosocial support and possible social transition for pre-pubescent children (5-7). As children enter the period of early development of secondary sex characteristics (Tanner 2 or 3 staging), guidelines recommend the use of gonadotropin releasing hormone (GnRH) agonists to suppress continued puberty. The goals of hormone suppression are to minimize dysphoria and to facilitate gender affirmation later in life (6, 7). Both guidelines suggest initiating cross-sex hormonal treatments around age 16 but acknowledge

that in some cases this may be appropriate even earlier (6-8). For all the interventions suggested, access to care and affordability vary across countries, health systems, and insurance plans (5).

It is important to keep in mind that existing practice guidelines for puberty suppression and gender affirming hormonal treatment are primarily based on consensus rather than high quality empirical data (6-13). The authors of these guidelines point out a lack of good quality evidence in identifying the optimal age at which gender affirming treatments should be initiated (8, 9, 11).

Most available studies addressing the gender affirmation care offered to TGD children and adolescents were based in individual clinics and included relatively small numbers (range: 25-187) of participants (14-16). Moreover, little is known about the typical course of events from initial presentation of TGD children to initiation of gender affirming care (13, 15-23). With the knowledge that the TGD population is growing, and increasing proportions of TGD individuals are presenting at an earlier age there is a need for large scale longitudinal studies investigating patterns and determinants of TGD-specific care in children and adolescents (24-28).

With these considerations in mind, the purpose of the present study is to examine the likelihood and predictors of receiving a TGD-specific diagnosis and receipt of gender-affirming hormonal therapy (GAHT), including GnHR agonists, among children who express gender variant behavior. In performing this analysis, we used data from a large cohort of TGD youth who received care within three integrated health systems in the United States.

Methods

This study utilizes data from the Study of Transition, Outcomes, and Gender (STRONG) cohort. The STRONG cohort includes participants from Kaiser Permanente (KP) integrated health systems in Georgia, Northern California, and Southern California. The three KP sites collectively provide comprehensive health care to over 8.8 million individuals (29, 30). The Emory University Rollins School of Public Health served as the coordinating center. The study protocol received approvals from Institutional Review Boards of all four institutions. The details of STRONG cohort ascertainment and data collection were described in previous publications (12, 27, 31). For the purposes of the current analyses, participants were identified in the electronic medical record (EMR) from January 1, 2006, through December 31, 2014, by searching for keywords reflecting gender diverse behaviors such as "transgender," "gender identity," and "gender dysphoria." Each participant's "index date" was defined based on the first evidence of gender diverse behaviors mentioned in the notes. All notes were reviewed to confirm eligibility.

The analytic dataset for the purposes of the current study was limited to participants who at index date were <18 years of age, and had evidence of gender diverse behavior, but did not have a TGD-specific diagnosis and had not received any TGD-related treatment. Participants who sex recorded at birth could not be determined (n=14) were excluded from the analyses. Two types of events of interest were ascertained during follow up: an assignment of the first TGD-specific diagnosis and receipt of gender-affirming hormonal therapy.

The TGD-specific diagnoses were based on the *International Classification of Diseases, Ninth Edition* (ICD-9) and included codes for conditions such as "transsexualism" (Code 302.5) and "gender identity disorder in children" (Code 302.6). GAHT receipt was determined from

pharmacy records and date of therapy initiation was based on the first ordered prescription for a medication used for puberty suppression or for the purposes of feminization or masculinization.

The follow up for each participant extended from the index date until the event of interest (diagnostic code or first ordered GAHT prescription, depending on the analysis), disenrollment from Kaiser Permanente, or end of follow up (December 31, 2014). Kaplan Meier curves were constructed to compare timing and occurrence of TGD diagnosis and GAHT initiation across subgroups of participants. The independent variables in these analyses included age category at index data (categorized as 3-9, 10-14 and 15+ years), recorded sex at birth (RMAB vs. RFAB), and race/ethnicity (Non-Hispanic whites vs. other race/ethnicity).

Multivariable Cox proportional hazards models were used to evaluate the associations of all three independent variables (sex recorded at birth, age and race/ethnicity) considered individually and simultaneously with each event of interest. The result of Cox models were expressed as crude and adjusted hazard ratios (HRs) and the corresponding 95% confidence intervals. All models were evaluated for validity of proportional hazard assumptions. If proportional hazard assumptions were violated, stratified Cox models were used. The data analyses were performed using SAS® Software Version 9.4 (SAS Institute Inc., Cary, NC).

Results

After applying eligibility criteria (Figure 1), 958 children were included in final analysis dataset (Table 1). Of those, 431 individuals were recorded as male at birth (RMAB) and 527 individuals were recorded as female at birth (RFAB). Children less than 10 years of age at index date represented 21% of the total cohort, 30% of the RMAB group and 14% of the RFAB group. In both the RMAB and RFAB groups, non-Hispanic whites made up over 45% of the children. A

majority of individuals received care at KP Northern California. Of the total analytic cohort, 29% of participants received a TGD diagnosis and 25% were prescribed GAHT during follow-up.

Compared to their RFAB counterparts a lower proportion of RMAB children and adolescents received a TGD diagnosis (24% vs. 33%) and initiated GAHT (14% vs. 33%) during follow up (Table 1). Rates of both TGD diagnosis and GAHT receipt were also significantly different in the two groups (Figure 2). After controlling for other variables (Table 2), the difference in TGD diagnosis rates between RMAB and RFAB was attenuated (adjusted HR=1.3; 95% CI: 1.0-1.7), but the difference in GAHT receipt remained pronounced (adjusted HR=2.5; 95% CI: 1.8-3.3).

Compared to their non-Hispanic white counterparts, children of minority races/ethnicities were less likely to receive a TGD diagnosis (26% vs. 33%) or be prescribed GAHT (21% vs. 29%) during follow up (Figure 3) and the time to TGD diagnosis and GAHT were also significantly different in the two groups (Figure 3). Controlling for other variables (Table 2), the difference in TGD diagnosis rates were unclear (adjusted HR=0.8; 95% CI: 0.6-1.0) while the different in GAHT receipt persisted (adjusted HR=0.6; 95% CI: 0.5-0.8).

Across the three age-at-index groups, children identified at an earlier age were less likely to receive a TGD diagnosis (3-9 years: 16%, 10-14 years: 28%, >15 years: 37%) and less likely to be prescribed GAHT (4% vs. 24% vs. 34%) during follow-up (Figure 4). Controlling for other variables (Table 2), the differences in TGD diagnosis rates remained pronounced across the three groups; using the youngest age group (3-9 years) as reference, the adjusted HRs (95% CI) were 2.0 (1.3-3.0) for age 10-14 years and 2.7 (1.8-3.9) for age 15+ years. The proportional hazard assumption for the age variable was violated in the analyses that used GAHT initiation as

the endpoint of interest, and for this reason the corresponding adjusted HR estimates across the age groups were not obtained (Table 2).

Discussion

This electronic health record-based cohort study nested in three large integrated health systems demonstrated that the majority of children who present with gender diversity do not receive a TGD diagnosis, and most do not appear to require GAHT. We also observed several notable differences in the rates of TGD diagnosis receipt and GAHT initiation across demographic categories of participants. Our results need to be viewed in the context of similar findings reported previously in European research (16, 23).

Two similarly designed, but non-overlapping, studies performed a follow up assessment of children treated for gender dysphoria at a specialized clinic in the Netherlands (16, 23). The first study approached 77 children who had been referred to a gender-specific clinic between 1989 and 2005 for gender dysphoria at less than 12 years of age at initial presentation (16). After an average follow up of ten years , 27% of the initial cohort "persisted" in experiencing gender dysphoria; however this result may have been affected the relatively high (30%) proportion of participants who did not respond to the survey (16). The authors also reported that individuals whose gender dysphoria persisted had more extreme gender dysphoria observed during childhood and were more likely to meet criteria for a TGD-diagnosis during childhood (16).

The second Dutch study originated from the same clinic, but sampled a different group of 127 adolescents between 2000 and 2008. As in the earlier study, participants received a TGD-specific diagnosis at less than 12 years of age and were followed up at 15 years of age or older (23). This study reported 37% of adolescents in the cohort overall persisted in gender dysphoria

at follow-up, with a still high non-response rate of 22% who were counted by the study as no longer experience gender dysphoria (23). Additionally, this study observed that several factors were associated with gender dysphoria persistence, including more pronounced symptoms of gender dysphoria, older age at presentation, and those individuals who were RFAB (23).

Both Dutch studies found that the majority of their participants did not experience gender dysphoria beyond puberty. This is consistent with our observation that less than one-third of children presenting with gender diverse behaviors received a TGD diagnosis and only about one-quarter initiated hormone therapy during follow up. The Dutch researchers also reported a greater likelihood of gender dysphoria persistence in children who presented at an older age and among RFAB participants; both results in agreement with our findings.

Perhaps the most important methodological feature of our study compared to previous research is the use of system-wide cohort ascertainment that was not limited to a particular clinical center. The de-identified data permitted inclusion of all eligible persons in the analyses, as participation did not require subject opt-in. In addition, the keyword-based approach to identify eligible study participants offered a rare opportunity to evaluate the course of events in children at earlier stages of gender variant behavior, which is rarely possible in specialized clinic-based studies.

It is worth noting that the methodological features of our study can be viewed as both its strengths and its weaknesses. As the analyses were based exclusively on the information obtained from medical records this precluded collection of patient- and family-reported measures. For this reason, limitations of our analyses include the lack of data on social environment or psychological support, and the inability to distinguish children who identify as transgender from those who present with non-binary or other gender non-conforming identities. Further, TGD

children enrolled in integrated health care systems come from primarily families with health insurance and may not be representative of the TGD population in the United States. On the other hand, this cohort does include patients enrolled in Medicaid plans, insuring that at least some of the study participants come from populations with lower socioeconomic status.

In summary, our analyses demonstrate that TGD adolescents are more likely to receive a gender dysphoria diagnosis or require hormone therapy compared to younger children. We also observed that both diagnosis receipt and treatment initiation were more common among non-Hispanic whites and RFAB children relative to their respective counterparts. These results indicate that even in the presence of similar access to care, utilization and timing of services may differ across groups of gender diverse children and adolescents. Future studies should explore the possible reasons for the observed differences by recruiting a cohort with a wider range of sociodemographic characteristics. Perhaps the most important next step in this area of research is to compare health outcomes and quality of life among TGD children and adolescents who began receiving care at different ages. These types of data are needed to inform clinical practice and facilitate development of evidence-based guidelines.

References

1. Pleak RR. Gender identity issues in youth: opportunities, terminologies, histories, and advancements. *Child Adolesc Psychiatr Clin N Am* 2011;20(4):601-25.
2. American Psychiatric Association., American Psychiatric Association. DSM-5 Task Force. *Diagnostic and statistical manual of mental disorders : DSM-5*. 5th ed. Washington, D.C.: American Psychiatric Association; 2013.
3. Cohen-Kettenis PT, Pfafflin F. The DSM diagnostic criteria for gender identity disorder in adolescents and adults. *Arch Sex Behav* 2010;39(2):499-513.
4. Beek TF, Cohen-Kettenis PT, Kreukels BP. Gender incongruence/gender dysphoria and its classification history. *Int Rev Psychiatry* 2016;28(1):5-12.
5. Shumer DE, Spack NP. Current management of gender identity disorder in childhood and adolescence: guidelines, barriers and areas of controversy. *Curr Opin Endocrinol Diabetes Obes* 2013;20(1):69-73.
6. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *Endocr Pract* 2017;23(12):1437.
7. Coleman E, Bockting W, Botzer M, et al. Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People, Version 7. *International Journal of Transgenderism* 2012;13(4):165-232.
8. Olson J, Garofalo R. The peripubertal gender-dysphoric child: puberty suppression and treatment paradigms. *Pediatr Ann* 2014;43(6):e132-7.
9. Costa R, Carmichael P, Colizzi M. To treat or not to treat: puberty suppression in childhood-onset gender dysphoria. *Nat Rev Urol* 2016;13(8):456-62.
10. de Vries AL, Cohen-Kettenis PT. Clinical management of gender dysphoria in children and adolescents: the Dutch approach. *J Homosex* 2012;59(3):301-20.
11. Khatchadourian K, Amed S, Metzger DL. Clinical management of youth with gender dysphoria in Vancouver. *J Pediatr* 2014;164(4):906-11.
12. Owen-Smith AA, Gerth J, Sineath RC, et al. Association Between Gender Confirmation Treatments and Perceived Gender Congruence, Body Image Satisfaction, and Mental Health in a Cohort of Transgender Individuals. *J Sex Med* 2018;15(4):591-600.
13. Menino DD, Katz-Wise SL, Vetters R, et al. Associations Between the Length of Time from Transgender Identity Recognition to Hormone Initiation and Smoking Among Transgender Youth and Young Adults. *Transgend Health* 2018;3(1):82-7.
14. Smith YL, van Goozen SH, Kuiper AJ, et al. Transsexual subtypes: clinical and theoretical significance. *Psychiatry Res* 2005;137(3):151-60.
15. Steensma TD, Biemond R, de Boer F, et al. Desisting and persisting gender dysphoria after childhood: a qualitative follow-up study. *Clin Child Psychol Psychiatry* 2011;16(4):499-516.
16. Wallien MS, Cohen-Kettenis PT. Psychosexual outcome of gender-dysphoric children. *J Am Acad Child Adolesc Psychiatry* 2008;47(12):1413-23.
17. Zuger B. Early effeminate behavior in boys. Outcome and significance for homosexuality. *J Nerv Ment Dis* 1984;172(2):90-7.
18. Steensma TD, van der Ende J, Verhulst FC, et al. Gender variance in childhood and sexual orientation in adulthood: a prospective study. *J Sex Med* 2013;10(11):2723-33.
19. Tuerk C. Considerations for affirming gender nonconforming boys and their families: new approaches, new challenges. *Child Adolesc Psychiatr Clin N Am* 2011;20(4):767-77.

20. Fast AA, Olson KR. Gender Development in Transgender Preschool Children. *Child Dev* 2018;89(2):620-37.
21. Golombok S, Rust J, Zervoulis K, et al. Developmental trajectories of sex-typed behavior in boys and girls: a longitudinal general population study of children aged 2.5-8 years. *Child Dev* 2008;79(5):1583-93.
22. Martin CL, Ruble DN. Patterns of gender development. *Annu Rev Psychol* 2010;61:353-81.
23. Steensma TD, McGuire JK, Kreukels BP, et al. Factors associated with desistence and persistence of childhood gender dysphoria: a quantitative follow-up study. *J Am Acad Child Adolesc Psychiatry* 2013;52(6):582-90.
24. Becerra-Fernandez A, Rodriguez-Molina JM, Asenjo-Araque N, et al. Prevalence, Incidence, and Sex Ratio of Transsexualism in the Autonomous Region of Madrid (Spain) According to Healthcare Demand. *Arch Sex Behav* 2017;46(5):1307-12.
25. Wiepjes CM, Nota NM, de Blok CJM, et al. The Amsterdam Cohort of Gender Dysphoria Study (1972-2015): Trends in Prevalence, Treatment, and Regrets. *J Sex Med* 2018;15(4):582-90.
26. Blosnich JR, Brown GR, Shipherd Phd JC, et al. Prevalence of gender identity disorder and suicide risk among transgender veterans utilizing veterans health administration care. *Am J Public Health* 2013;103(10):e27-32.
27. Quinn VP, Nash R, Hunkeler E, et al. Cohort profile: Study of Transition, Outcomes and Gender (STRONG) to assess health status of transgender people. *BMJ Open* 2017;7(12):e018121.
28. Aydin D, Buk LJ, Partoft S, et al. Transgender Surgery in Denmark From 1994 to 2015: 20-Year Follow-Up Study. *J Sex Med* 2016;13(4):720-5.
29. Gordon NP. How Does the Adult Kaiser Permanente Membership in Northern California Compare with the Larger Community? Oakland, CA: Kaiser Permanente Northern California Division of Research, 2006.
30. Koebnick C, Langer-Gould AM, Gould MK, et al. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. *Perm J* 2012;16(3):37-41.
31. Becerra-Culqui TA, Liu Y, Nash R, et al. Mental Health of Transgender and Gender Nonconforming Youth Compared With Their Peers. *Pediatrics* 2018;141(5).

Table 1. Selected participant characteristics by recorded sex at birth

Participant characteristics		RMAB N (%)	RFAB N (%)	Total N (%)
Age at index date				
	3-9 yrs.	131 (30%)	74 (14%)	205 (21%)
	10-14 yrs.	128 (30%)	172 (33%)	300 (31%)
	15+ yrs.	172 (40%)	281 (53%)	453 (47%)
Race/Ethnicity				
	White	196 (45%)	277 (53%)	473 (49%)
	Black	42 (10%)	44 (8%)	86 (9%)
	Asian	30 (7%)	47 (9%)	77 (8%)
	Hispanic	128 (30%)	130 (25%)	258 (27%)
	Other	5 (1%)	8 (2%)	13 (1%)
	Unknown	30 (7%)	21 (4%)	51 (5%)
Site				
	Georgia	12 (3%)	15 (3%)	27 (3%)
	Northern California	264 (61%)	340 (65%)	604 (63%)
	Southern California	155 (36%)	172 (33%)	327 (34%)
TGD diagnosis during follow-up				
	Yes	105 (24%)	176 (33%)	281 (29%)
	No	326 (76%)	351 (67%)	677 (71%)
GAHT initiation during follow-up				
	Yes	60 (14%)	176 (33%)	236 (25%)
	No	371 (86%)	351 (67%)	722 (75%)

Table 2. Results of Cox Proportional models evaluating associations between participant characteristics and each event of interest

Independent Variables	Crude HR	95% CI	Adjusted HR	95% CI
		Outcome: TGD-specific Diagnosis		
Recorded sex at birth				
Male (RMAB)	1.0	Reference	1.0	Reference
Female (RFAB)	1.5	1.2, 1.9	1.3	1.0, 1.6
Age at index date				
3-9 yrs.	1.0	Reference	1.0	Reference
10-14 yrs.	2.0	1.3, 3.0	2.0	1.3, 3.0
15+ yrs.	2.8	1.9, 4.1	2.7	1.8, 3.9
Race/ethnicity				
Non-Hispanic whites	1.0	Reference	1.0	Reference
Other groups	0.8	0.6, 1.0	0.8	0.6, 1.0
		Outcome: GAHT initiation*		
Recorded sex at birth				
Male (RMAB)	1.0		1.0	Reference
Female (RFAB)	3.0	2.2, 4.0	2.5	1.8, 3.3
Race/ethnicity				
Non-Hispanic whites	1.0	Reference	1.0	Reference
Other groups	0.6	0.5, 0.8	0.6	0.5, 0.8

*Model stratified on age due to violation of proportional hazards assumption for that variable

Figure 1. Inclusion and Exclusion of Individuals

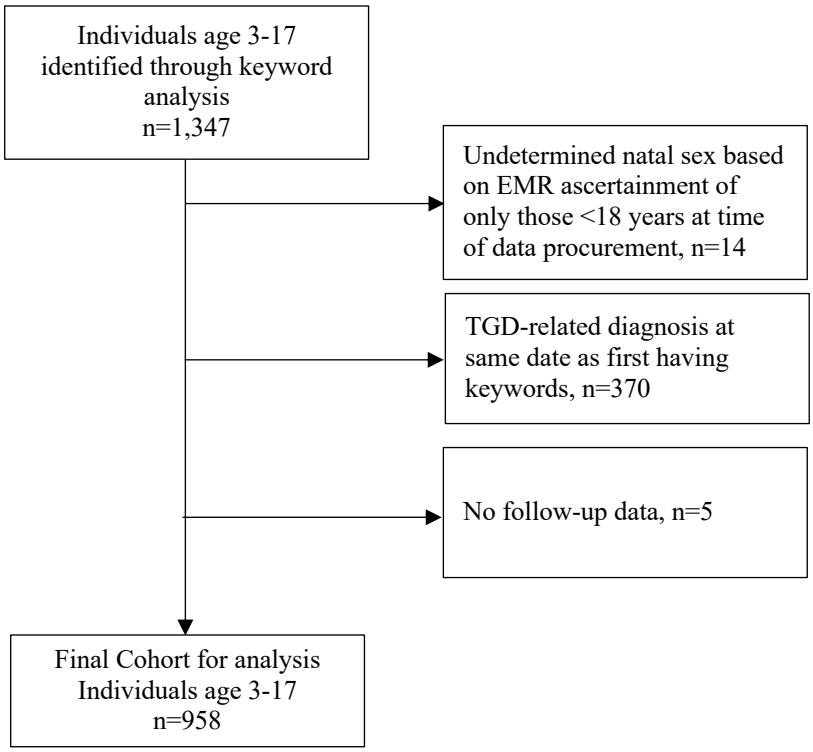
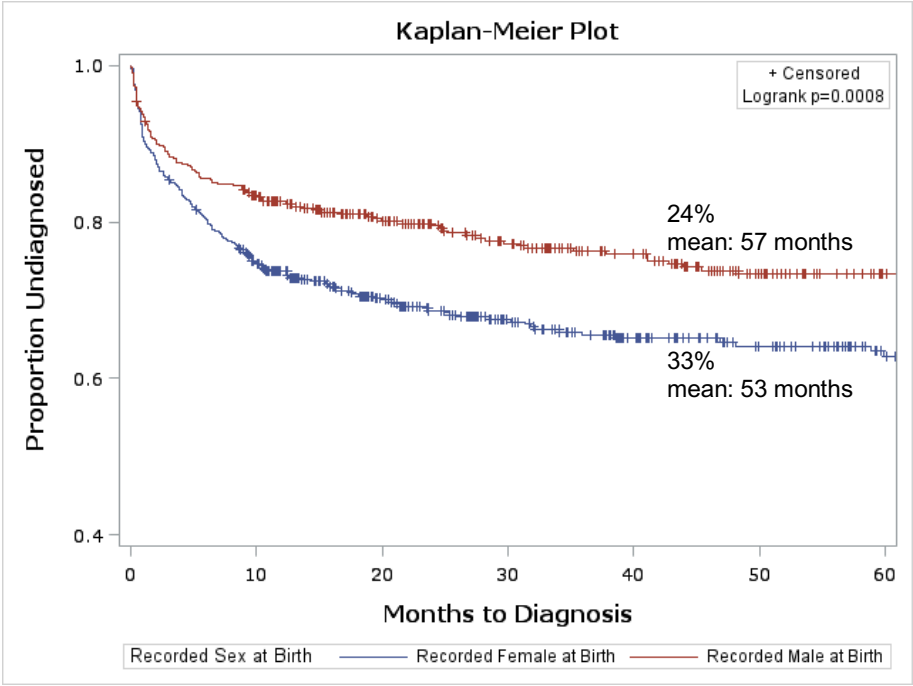


Figure 2. Kaplan Meier Time-to-Event Analysis Gender Recorded at Birth

Panel A. Outcome: Transgender-related Diagnosis



Panel B. Outcome: Gender-Affirming Hormonal Therapy

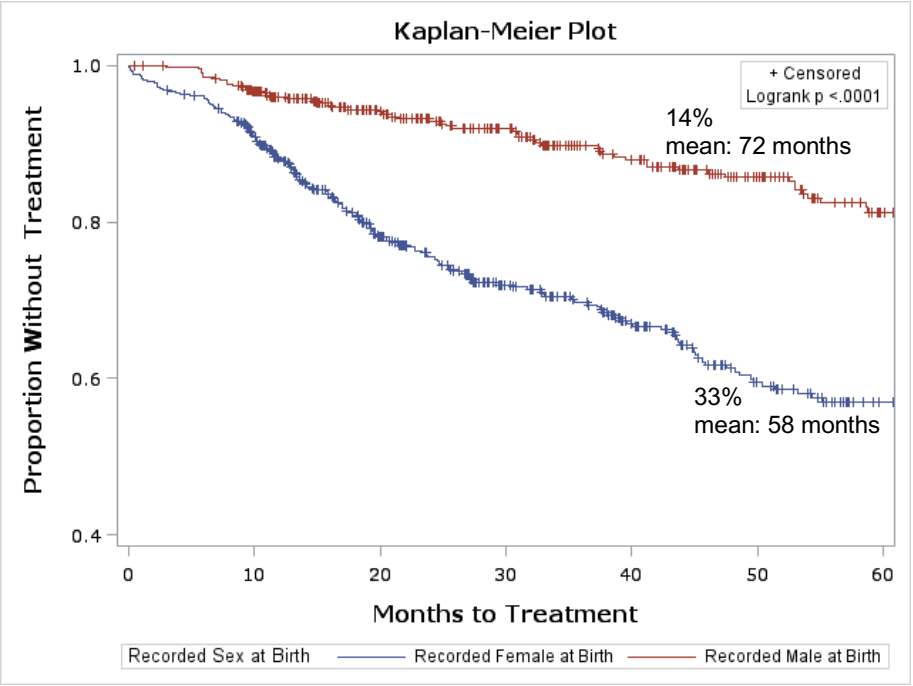
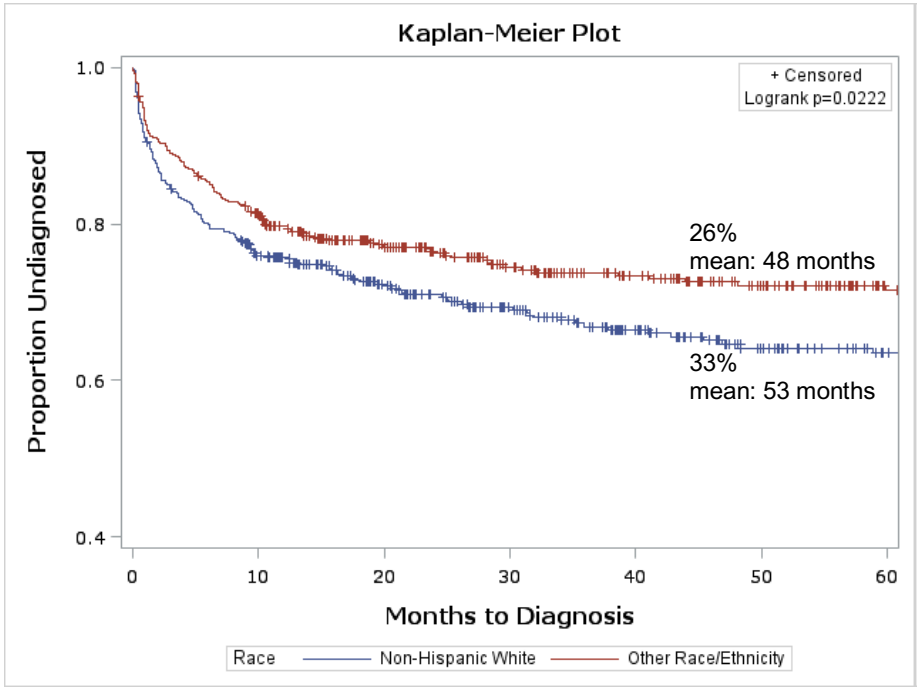


Figure 3. Kaplan Meier Time-to-Event Analysis Non-Hispanic White vs. Other Race/Ethnicity

Panel A. Outcome: Transgender-related Diagnosis



Panel B. Outcome: Gender-Affirming Hormonal Therapy

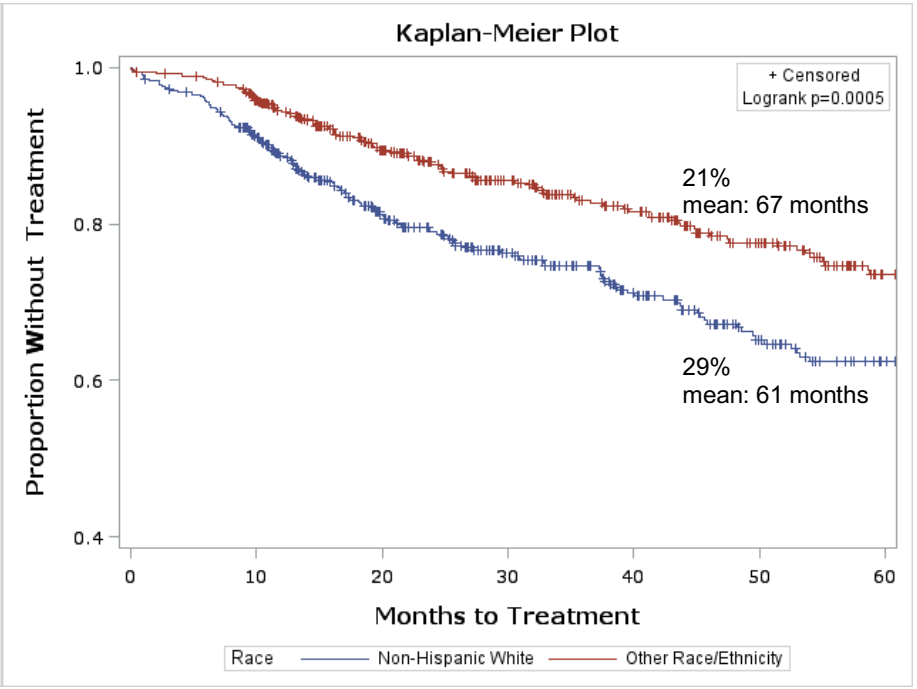
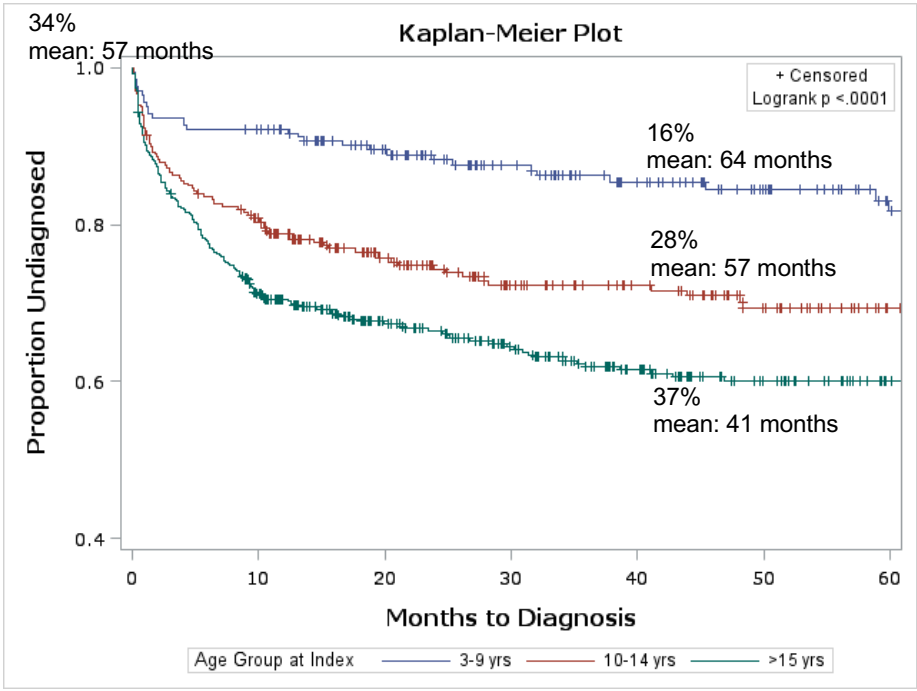


Figure 4. Kaplan Meier Time-to-Event Analysis by Age at Index Date: 3-9 yrs. vs. 10-14 yrs. vs. >15 yrs.

Panel A. Outcome: Transgender-related Diagnosis



Panel B. Outcome: Gender-Affirming Hormonal Therapy