**Table S1.** The Adolescent Psychotic-like Symptom Screener (APSS).

|  |  |
| --- | --- |
| Items | Abbreviation |
| 1. Some people believe that their thoughts can be read by another person. Have other people ever read your mind? | Mind reading |
| 2. Have you ever had messages sent just to you through TV or radio? | TV/radio |
| 3. Have you ever thought that people are following or spying on you? | Spying |
| 4. Have you ever heard voices or sounds that no one else can hear? | Auditory hallucinations |
| 5. Have you ever felt you were under the control of some special power? | Controlled |
| 6. Have you ever seen things that other people could not see? | Visual hallucinations |
| 7. Have you ever felt like you had extraspecial powers? | Grandiosity |

**Table S2.** The Neighborhood Collective Efficacy (NCE) scale.

|  |
| --- |
| Items |
| 1. The neighbors are kind and dependable |
| 2. The neighbors help each other |
| 3. The neighbors can be trusted |
| 4. The neighbors usually try to be helpful |
| 5. The neighbors get along with each other |

**Table S3.** A weighting approach to examine multiple mediators.

|  |  |
| --- | --- |
| Counterfactuals | Descriptions |
| *E[Ya\*Ma\*]* | A weighted average of the subjects with *A* = *a\** where each subject *i* is given a weight *P* (*A* = *a\**)/*P* (*A* = *a\**| *ci*) where *ci* denotes the actual covariate value for subject *i*. |
| *E[YaMa]* | A weighted average of the subjects with *A* = *a* where each subject *i* is given a weight *P* (*A* = *a*)/*P* (*A* = *a*| *ci*) where *ci* denotes the actual covariate value for subject *i*. |
| *E[YaMa\*]* | For each subject *i* with *Ai* = *a\**, an outcome model is fitted to obtain a predicted estimate of the outcome if the individual had had exposure *Ai* = *a* rather than *Ai* = *a\**, using the individual’s own values of the mediators and covariates. *E[YaMa\*]* can be obtained by taking a weighted average of these predicted values for subjects with *Ai* = *a\** where each subject *i* is given the weight *P* (*A* = *a\**)/*P* (*A* = *a\**| *ci*) where *ci* denotes the actual covariate value for subject *i*. The details of the outcome model we utilized are provided in the footnote below. |
| *E[YaMa\*] − E[Ya\*Ma\*]* | Marginal natural direct effect |
| *E[YaMa] − E[YaMa\*]* | Marginal natural indirect effect |

*A* = Exposure

*Yam* = A subject's counterfactual value for the outcome *Y* if the exposure *A* were set to *a* and the mediator *M* were set to *m*

*Ma* = A subject's counterfactual value for the mediator *M* if the exposure *A* were set to *a*

Additionally, we calculated a weight for censoring to address loss to follow-up. The product of the weights for exposure and censoring constituted the final weight, which was used to analyze the counterfactual values. We fitted the following outcome model:

*E* [Mental health outcome at age 16| Gender nonconformity at age 12, Loneliness, Bullying victimization, and Relationships with mother, father, and friends at age 14, Covariates at age 12]

=*a0* + *a1* Gender nonconformity at age 12 + *a2* Loneliness at age 14 + *a3* Bullying victimization at age 14

+ *a4* Relationship with mother at age 14 + *a5* Relationship with father at age 14 + *a6* Relationship with friends at age 14

+ *a7* Gender nonconformity at age 12 \* Loneliness at age 14

+ *a8* Gender nonconformity at age 12 \* Bullying victimization at age 14

+ *a9* Gender nonconformity at age 12 \* Relationship with mother at age 14

+ *a10* Gender nonconformity at age 12 \* Relationship with father at age 14

+ *a11* Gender nonconformity at age 12 \* Relationship with friends at age 14

+ *a12* Loneliness at age 14 \* Bullying victimization at age 14 + *a13* Covariates at age 12

Other potential interactions, e.g., Gender nonconformity at age 12 \* Loneliness at age 14 \* Bullying victimization at age 14, were not included in the model due to the limited statistical power. The confidence intervals for the direct and indirect effects were obtained by the normal approximation based on the 100 bootstrap samples.

**Table S4.** Models excluding relationships with mother, father, and friends at age 14.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Types of gender nonconformity | Age 12 | Age 14 | Depression*β* (95% CI) | Psychotic experiences*β* (95% CI) | Anxiety*β* (95% CI) |
| Gender nonconforming behavior | Not at all | Not at all | 0.00 [Reference] | 0.00[Reference] | 0.00 [Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.55(0.85, 2.25) | 0.23(0.12, 0.34) | 0.32(-0.07, 0.72) |
|  | Somewhat, sometimes, very, or often | Not at all | 0.34(-0.15, 0.82) | 0.04(-0.02, 0.09) | 0.03(-0.28, 0.34) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 2.26(1.05, 3.47) | 0.29(0.10, 0.48) | 0.47(-0.17, 1.12) |
| Wish to be of the other gender | Not at all | Not at all | 0.00[Reference] | 0.00[Reference] | 0.00[Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.81(1.20, 2.42) | 0.25(0.15, 0.34) | 0.48(0.11, 0.86) |
|  | Somewhat, sometimes, very, or often | Not at all | 0.48(-0.12, 1.07) | -0.003(-0.07, 0.06) | 0.13(-0.22, 0.48) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 1.77(0.60, 2.94) | 0.20(0.02, 0.39) | 0.24(-0.48, 0.97) |

Abbreviation: CI, confidence interval

Marginal structural model with weights accounted for covariate distributions between groups. The model included the interaction between gender nonconformity at ages 12 and 14. For variable selection, see the Covariates subsection of the Methods section. Missing data were handled using multiple imputation via chained equation.

**Table S5.** Models including puberty at age 12.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Types of gender nonconformity | Age 12 | Age 14 | Depression*β* (95% CI) | Psychotic experiences*β* (95% CI) | Anxiety*β* (95% CI) |
| Gender nonconforming behavior | Not at all | Not at all | 0.00 [Reference] | 0.00[Reference] | 0.00 [Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.60(0.89, 2.31) | 0.23(0.12, 0.34) | 0.33(-0.07, 0.73) |
|  | Somewhat, sometimes, very, or often | Not at all | 0.31(-0.17, 0.79) | 0.04(-0.02, 0.09) | 0.02(-0.29, 0.33) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 2.28(1.04, 3.51) | 0.28(0.10, 0.46) | 0.42(-0.21, 1.06) |
| Wish to be of the other gender | Not at all | Not at all | 0.00[Reference] | 0.00[Reference] | 0.00[Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.82(1.21, 2.42) | 0.24(0.15, 0.34) | 0.47(0.10, 0.84) |
|  | Somewhat, sometimes, very, or often | Not at all | 0.48(-0.12, 1.07) | -0.001(-0.06, 0.06) | 0.15(-0.21, 0.50) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 1.78(0.61, 2.94) | 0.20(0.02, 0.39) | 0.27(-0.47, 1.00) |

Abbreviation: CI, confidence interval

Marginal structural model with weights accounted for covariate distributions between groups. The model included the interaction between gender nonconformity at ages 12 and 14. For variable selection, see the Covariates subsection of the Methods section. Missing data were handled using multiple imputation via chained equation.

**Table S6.** Models including mental health outcomes at age 16 as dichotomous variables.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Types of gender nonconformity | Age 12 | Age 14 | DepressionOR (95% CI) | Psychotic experiencesOR (95% CI) |
| Gender nonconforming behavior | Not at all | Not at all | 1.00[Reference] | 1.00[Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.61(1.21, 2.15) | 1.70(1.30, 2.24) |
|  | Somewhat, sometimes, very, or often | Not at all | 1.14(0.88, 1.47) | 1.27(1.02, 1.58) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 2.07(1.35, 3.18) | 1.86(1.26, 2.74) |
| Wish to be of the other gender | Not at all | Not at all | 1.00[Reference] | 1.00[Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.79(1.39, 2.30) | 1.67(1.33, 2.11) |
|  | Somewhat, sometimes, very, or often | Not at all | 1.31(0.98, 1.77) | 0.92(0.71, 1.21) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 1.88(1.16, 3.05) | 1.32(0.82, 2.14) |

Abbreviations: OR, odds ratio; CI, confidence interval

Marginal structural model with weights accounted for covariate distributions between groups. The model included the interaction between gender nonconformity at ages 12 and 14. For variable selection, see the Covariates subsection of the Methods section. Missing data were handled using multiple imputation via chained equation.

**Table S7.** Models including a dislike of their sexual anatomy because of the incongruence with experienced gender at ages 12 and 14.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Types of gender nonconformity | Age 12 | Age 14 | Depression*β* (95% CI) | Psychotic experiences*β* (95% CI) | Anxiety*β* (95% CI) |
| Dislike of their sexual anatomy because of the incongruence with experienced gender | Not at all | Not at all | 0.00[Reference] | 0.00[Reference] | 0.00[Reference] |
|  | Not at all | Somewhat, fairly, strongly, or very strongly | 1.78(1.02 , 2.54) | 0.26(0.14, 0.37) | 0.80(0.34, 1.26) |
|  | Somewhat, fairly, strongly, or very strongly | Not at all | -0.41(-0.88, 0.07) | 0.05(-0.01, 0.11) | 0.27(-0.06 , 0.60) |
|  | Somewhat, fairly, strongly, or very strongly | Somewhat, fairly, strongly, or very strongly | 0.53(-0.80 , 1.87) | 0.30(0.05 , 0.54) | 0.72(-0.31, 1.75) |

Abbreviations: CI, confidence interval

Marginal structural model with weights accounted for covariate distributions between groups. The model included the interaction between gender nonconformity at ages 12 and 14. For variable selection, see the Covariates subsection of the Methods section. Missing data were handled using multiple imputation via chained equation.

**Table S8.** Heterogeneity across gender: models including mental health outcomes at age 16 as continuous variables and interactions between sex and gender nonconformity.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | Depression*β* (95% CI) | Psychotic experiences*β* (95% CI) | Anxiety*β* (95% CI) |
| Types of gender nonconformity | Age 12 | Age 14 | Female | Male | Female | Male | Female | Male |
| Gender nonconforming behavior | Not at all | Not at all | 0.00 [Reference] | 0.00[Reference] | 0.00 [Reference] | 0.00 [Reference] | 0.00[Reference] | 0.00 [Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.71(0.91, 2.52) | -0.27(-1.42, 0.87) | 0.21(0.10, 0.31) | 0.23(0.04, 0.43) | 0.54(0.06, 1.03) | -0.52(-1.16, 0.12) |
|  | Somewhat, sometimes, very, or often | Not at all | 0.48(-0.35, 1.32) | -1.42(-2.03, -0.81) | 0.06(-0.03, 0.15) | -0.01(-0.08, 0.07) | 0.07(-0.44, 0.57) | -0.61(-1.04, -0.18) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 1.46(0.36, 2.56) | 1.41(-0.85, 3.66) | 0.14(0.01, 0.27) | 0.42(0.05, 0.78) | 0.06(-0.57, 0.69) | 0.25(-0.89, 1.38) |
| Wish to be of the other gender | Not at all | Not at all | 0.00[Reference] | 0.00[Reference] | 0.00[Reference] | 0.00[Reference] | 0.00[Reference] | 0.00[Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.58(0.86, 2.30) | 0.39(-0.63, 1.42) | 0.20(0.10, 0.29) | 0.25(0.09, 0.42) | 0.38(-0.06, 0.82) | -0.15(-0.78, 0.47) |
|  | Somewhat, sometimes, very, or often | Not at all | 1.08(0.05, 2.10) | -1.71(-2.36, -1.07) | 0.02(-0.08, 0.12) | -0.06(-0.14, 0.03) | -0.08(-0.64, 0.48) | -0.41(-0.89, 0.08) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 1.97(0.56, 3.39) | 0.13(-1.59, 1.84) | 0.15(-0.03, 0.35) | 0.20(-0.09, 0.50) | 0.22(-0.64, 1.07) | -0.37(-1.49, 0.75) |

Abbreviation: CI, confidence interval

We fitted the following outcome model:

*E* [Mental health outcome at age 16| Gender nonconformity at age 12, Gender nonconformity at age 14, Sex]

=*b0* + *b1* Gender nonconformity at age 12 + *b2* Gender nonconformity at age 14 + *b3* Sex

+ *b4* Gender nonconformity at age 12 \* Gender nonconformity at age 14

+ *b5* Gender nonconformity at age 12 \* Sex

+ *b6* Gender nonconformity at age 14 \* Sex

+ *b7* Gender nonconformity at age 12 \* Gender nonconformity at age 14 \* Sex

For variable selection, see the Covariates subsection of the Methods section. Missing data were handled using multiple imputation via chained equation.

**Table S9.** Heterogeneity across gender: models including mental health outcomes at age 16 as dichotomous variables and interactions between sex and gender nonconformity.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  | DepressionOR (95% CI) | Psychotic experiencesOR (95% CI) |
| Types of gender nonconformity | Age 12 | Age 14 | Female | Male | Female | Male |
| Gender nonconforming behavior | Not at all | Not at all | 1.00 [Reference] | 1.00[Reference] | 1.00 [Reference] | 1.00 [Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.57(1.17, 2.12) | 0.81(0.47, 1.38) | 1.58(1.19, 2.10) | 1.33(0.83, 2.11) |
|  | Somewhat, sometimes, very, or often | Not at all | 1.17(0.82, 1.67) | 0.53(0.37, 0.76) | 1.29(0.93, 1.80) | 0.91(0.67, 1.22) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 1.52(1.01, 2.27) | 1.42(0.66, 3.08) | 1.63(1.11, 2.39) | 1.51(0.76, 3.00) |
| Wish to be of the other gender | Not at all | Not at all | 1.00[Reference] | 1.00[Reference] | 1.00[Reference] | 1.00[Reference] |
|  | Not at all | Somewhat, sometimes, very, or often | 1.66(1.26, 2.19) | 1.01(0.64, 1.60) | 1.53(1.18, 1.98) | 1.34(0.90, 1.98) |
|  | Somewhat, sometimes, very, or often | Not at all | 1.59(1.07, 2.35) | 0.48(0.30, 0.76) | 1.08(0.74, 1.59) | 0.56(0.38, 0.82) |
|  | Somewhat, sometimes, very, or often | Somewhat, sometimes, very, or often | 1.91(1.18, 3.09) | 1.01(0.43, 2.38) | 1.15(0.70, 1.89) | 1.11(0.52, 2.41) |

Abbreviation: OR, odds ratio; CI, confidence interval

We fitted the following outcome model:

logit{*P*(Mental health outcome at age 16 = 1| Gender nonconformity at age 12, Gender nonconformity at age 14, Sex)}

=*b0* + *b1* Gender nonconformity at age 12 + *b2* Gender nonconformity at age 14 + *b3* Sex

+ *b4* Gender nonconformity at age 12 \* Gender nonconformity at age 14

+ *b5* Gender nonconformity at age 12 \* Sex

+ *b6* Gender nonconformity at age 14 \* Sex

+ *b7* Gender nonconformity at age 12 \* Gender nonconformity at age 14 \* Sex

For variable selection, see the Covariates subsection of the Methods section. Missing data were handled using multiple imputation via chained equation.

**Table S10.** Mediating role of loneliness, bullying victimization, and relationships with mother, father, and friends at age 14 on the association between gender nonconformity at age 12 and mental health outcomes at age 16

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Type of gender nonconformity | Outcome | Direct effect(95% bootstrap CI) | Indirect effect(95% bootstrap CI) | Proportion mediated, % |
| Gender nonconforming behavior | Depression | 0.43 (-0.31, 1.16) | 0.18 (-0.15, 0.51) | 29.8 |
|  | Psychotic experiences | -0.03 (-0.12, 0.06) | 0.0001 (-0.03, 0.03) | NAa |
|  | Anxiety | 0.07 (-0.38, 0.52) | -0.08 (-0.26, 0.11) | NAa |
| Wish to be of the other gender | Depression | 0.56 (-0.24, 1.36) | 0.20 (-0.29, 0.69) | 26.0 |
|  | Psychotic experiences | 0.04 (-0.08, 0.16) | 0.01 (-0.05, 0.06) | 18.4 |
|  | Anxiety | 0.34 (-0.18, 0.85) | 0.03 (-0.23, 0.29) | 8.0 |

Abbreviation: CI, confidence interval

To account for exposure-mediator and mediator-mediator interactions, a weighting approach was employed to simultaneously examine all mediators, instead of evaluating each mediator individually. We fitted the following outcome model:

*E* [Mental health outcome at age 16| Gender nonconformity at age 12, Loneliness, Bullying victimization, and Relationships with mother, father, and friends at age 14, Covariates at age 12]

=*a0* + *a1* Gender nonconformity at age 12 + *a2* Loneliness at age 14 + *a3* Bullying victimization at age 14

+ *a4* Relationship with mother at age 14 + *a5* Relationship with father at age 14 + *a6* Relationship with friends at age 14

+ *a7* Gender nonconformity at age 12 \* Loneliness at age 14

+ *a8* Gender nonconformity at age 12 \* Bullying victimization at age 14

+ *a9* Gender nonconformity at age 12 \* Relationship with mother at age 14

+ *a10* Gender nonconformity at age 12 \* Relationship with father at age 14

+ *a11* Gender nonconformity at age 12 \* Relationship with friends at age 14

+ *a12* Loneliness at age 14 \* Bullying victimization at age 14 + *a13* Covariates at age 12

Other potential interactions, e.g., Gender nonconformity at age 12 \* Loneliness at age 14 \* Bullying victimization at age 14, were not included in the model due to the limited statistical power.

The CIs for the direct and indirect effects were obtained by the normal approximation based on the 100 bootstrap samples.

aNot estimable because the direct and indirect effects were in opposite directions.

**Table S11.** Sensitivity analysis for the mediation: depression evaluated by the SMFQ removing the loneliness item.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Type of gender nonconformity | Outcome | Direct effect(95% bootstrap CI) | Indirect effect(95% bootstrap CI) | Proportion mediated, % |
| Gender nonconforming behavior | Depression | 0.41 (-0.30, 1.12) | 0.17 (-0.14, 0.49) | 30.0 |
| Wish to be of the other gender | Depression | 0.55 (-0.21, 1.32) | 0.20 (-0.27, 0.67) | 26.4 |

Abbreviation: SMFQ, Short Mood and Feelings Questionnaire; CI, confidence interval

To account for exposure-mediator and mediator-mediator interactions, a weighting approach was employed to simultaneously examine all mediators, instead of evaluating each mediator individually. We fitted the following outcome model:

*E* [Depression at age 16| Gender nonconformity at age 12, Loneliness, Bullying victimization, and Relationships with mother, father, and friends at age 14, Covariates at age 12]

=*a0* + *a1* Gender nonconformity at age 12 + *a2* Loneliness at age 14 + *a3* Bullying victimization at age 14

+ *a4* Relationship with mother at age 14 + *a5* Relationship with father at age 14 + *a6* Relationship with friends at age 14

+ *a7* Gender nonconformity at age 12 \* Loneliness at age 14

+ *a8* Gender nonconformity at age 12 \* Bullying victimization at age 14

+ *a9* Gender nonconformity at age 12 \* Relationship with mother at age 14

+ *a10* Gender nonconformity at age 12 \* Relationship with father at age 14

+ *a11* Gender nonconformity at age 12 \* Relationship with friends at age 14

+ *a12* Loneliness at age 14 \* Bullying victimization at age 14 + *a13* Covariates at age 12

Other potential interactions, e.g., Gender nonconformity at age 12 \* Loneliness at age 14 \* Bullying victimization at age 14, were not included in the model due to the limited statistical power.

The CIs for the direct and indirect effects were obtained by the normal approximation based on the 100 bootstrap samples.