

MILLIMAN REPORT

Evaluation of Progyny's Methodology Used in their Fertility Outcomes Study

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I. EXECUTIVE SUMMARY

SCOPE AND PURPOSE

Progyny, Inc. (Progyny) specializes in fertility and family building benefit solutions in the United States. They provide comprehensive fertility benefits including diagnostic testing, medical services and medications required for a member's full course of fertility treatment, care management and patient care advocacy and support.

Progyny routinely measures how the outcomes of patients managed through its fertility program fare in comparison to national benchmarks. Progyny engaged Milliman, Inc. (Milliman) to evaluate the methodology Progyny used to compare its outcomes to national benchmarks. The results of Progyny's study can be found here: <https://progyny.com/for-employers/benefits-at-work/>. In this report, Progyny's study is referred to as the Progyny Fertility Outcomes Study. This report opines on the appropriateness and reasonability of the methodology Progyny used in its Fertility Outcomes Study and does not provide any opinions about Progyny's clinical model or its approach to managing patient cases. This report includes our evaluation of methodology for Progyny's study, which compares Progyny's fertility outcomes to two benchmarks. This report comments on the following:

- Reasonableness of the indicators Progyny used to measure the efficacy of its fertility management program
- Appropriateness of each measure for calculating fertility outcomes
- Differences assessed between Progyny data and benchmark data
- Methodologies Progyny used to measure clinical outcomes and program efficacy

The five clinical outcomes reviewed in the Progyny Fertility Outcome Study include:

- Pregnancy rate per in vitro fertilization (IVF) transfer
- IVF miscarriage rate
- IVF live birth rate
- Single embryo transfer (SET) rate
- IVF multiples rate

SUMMARY OF FINDINGS

We focused our review on the measures used to evaluate fertility outcomes, the time periods used in the analysis and the consistency of the methodology used to compare the different populations. Overall, we find the general methodology used to compare Progyny's fertility clinical outcomes to national benchmarks to be appropriate and reasonable to measure program effectiveness. Progyny's methodology follows an approach where clinical fertility outcomes for internal (Progyny) and external (non-Progyny) groups were adjusted for age and compared to each other. Analyzing the drivers of Progyny's clinical outcomes with respect to their product offering was not within the scope of this analysis.

In the fertility space we consider the five measures studied by Progyny to be sufficient to measure the efficacy of a fertility program. These measures are commonly used in the literature to measure pregnancy success, health of the pregnancy, and health of the baby.

Progyny's analysis relied on data from the Centers for Disease Control and Prevention (CDC), the Society for Assisted Reproductive Technology (SART), and Progyny in-network providers. The four populations included in the Progyny Fertility Outcome Study are; 1) the Progyny population, 2) the non-Progyny in-network population, 3) the non-Progyny national population, and 4) the non-Progyny out-of-network population. Progyny's methodology adjusts for differences in age between the populations, which is critical for isolating differences in fertility outcomes between the populations. Because fertility generally decreases with age, age is considered one of the strongest predictors in determining success rates with fertility treatments.¹ While the methodology could be improved if there were more factors accounted for in the analysis, such as infertility diagnosis, use of donor egg, preimplantation genetic testing (PGT), and fertility insurance coverage, this is not currently possible due to the way the additional factors are reported by CDC and SART. While the CDC collects this data, they do not report it by different age brackets, limiting the ability to compare outcomes data on these variables. Although one could normalize for these factors without accounting for age, age is one of the most critical factors to consider.

¹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3017326/>

In its outcomes study, Progyny uses the most recent data available from Progyny and external sources for the comparison. As of the date of this report, Progyny reported outcomes from 2021. However, the most recent and complete data available from CDC and SART represents data from 2019 to 2020. Some of the differences in fertility outcomes may also be attributed to the difference in time periods used. While Progyny data is from 2021, the data used for the comparator populations (the non-Progyny in-network population, the non-Progyny out-of-network population, and the non-Progyny national population) ranges from 2019 to 2020, depending on the measure's availability. As some of the fertility outcomes included in the study have been improving year-over-year nationally, those improvements should be considered while analyzing Progyny's report. As Progyny uses more recent data than available from CDC and SART, these annual improvements may be contributing to the difference between Progyny and external populations. A best practice would be to compare datasets from the same time period. However, even when Progyny data from the same time period is compared to SART and CDC data, differences between Progyny versus non-Progyny in-network national outcomes are statistically significant and directionally consistent, as outlined in Table 1. Please note, Progyny is issuing the most up to date data for each metric and updates its reports as new data becomes available.

Table 1
Progyny's Fertility Outcomes Study
Comparison of Results by Time Period

Measure	Non-Progyny out-of-network clinic national rate	Non-Progyny all clinic national Rate	Non-Progyny in-network clinic national rate	Progyny 2021 (used in Fertility Outcomes Study)	Progyny 2020*
Pregnancy Rate (per Transfer) **	50.1%	54.1%	55.5%	63.0%	61.4%
Miscarriage Rate (per Pregnancy) **	19.5%	18.6%	18.3%	13.9%	13.8%
Live Birth Rate (per Transfer) ***	39.4%	42.7%	44.1%	54.3%	52.9%
SET Rate (per Transfer) **	63.3%	72.5%	75.6%	91.0%	90.1%
Multiples Rate (per Live Birth) ***	9.6%	7.4%	6.5%	2.5%	2.8%

*Milliman actuaries calculated the statistical significance of the difference between Progyny 2020 outcomes, and the non-Progyny in-network clinic national rate based on 1% significance. We determined the observed difference to be statistically significant, meaning there is a significantly low probability that the results between the two populations were achieved due to random variation / chance, but cannot comment on the origin of this difference. We assumed a normal distribution and conducted a one-tailed two proportion z-test to calculate statistical significance.

**Calculated based on the SART 2019 National Summary Report, finalized in 2022.

***Calculated based on CDC, 2020 National Summary and Clinic Data Sets, published in 2022.

Note: Progyny represents Progyny in-network provider clinic averages for Progyny members only

Progyny's analysis focuses exclusively on comparing clinical fertility outcomes of Progyny patients to non-Progyny populations. As such, our review similarly focuses on the methodology to compare clinical fertility outcomes between Progyny and external populations. Analyzing the drivers of Progyny's clinical outcomes with respect to their product offering was not within the scope of this analysis. Correspondingly, our review in this report is limited to the methodology used to calculate fertility outcomes and compare the Progyny population to external populations.

II. OVERVIEW OF PROGYNYS FERTILITY OUTCOMES STUDY

Based on information provided by Progyny, the following is our interpretation of Progyny's Fertility Outcomes Study.

Progyny's fertility benefit solution integrates active management of contracted healthcare providers and member support. Prior to joining Progyny's network, providers must meet a set of inclusion standards. Each member receives unlimited access to a dedicated Patient Care Advocate who provides support, education, and guidance on the fertility process. The fertility benefit is structured in a way that members do not exceed coverage limits in a given treatment cycle.

The Progyny Fertility Outcomes Study is a retrospective review of 2021 fertility outcomes of Progyny members compared to three benchmarks – the non-Progyny national average, the in-network average for all non-Progyny members, and the out-of-network average for all non-Progyny members. The measures include pregnancy rate per IVF transfer, IVF miscarriage rate, IVF live birth rate, SET rate, and IVF multiples rate. Further descriptions of the measures can be found in the Fertility Outcome Measures section of the report. The non-Progyny national average includes all non-Progyny members from both in-network and out-of-network providers. The second national benchmark includes members who went to providers in Progyny's network but are not Progyny members. Comparing Progyny members to non-Progyny members in the same provider network enables Progyny to distinguish between Progyny member outcomes and the outcomes associated with an identical provider network that excludes Progyny members. The third national benchmark includes members who went to providers outside of Progyny's network and are not Progyny members. Comparing non-Progyny member outcomes from in-network clinics to out-of-network clinics enables Progyny to distinguish between national outcomes based on network status.

DATA COLLECTION

The Progyny member outcomes are collected directly from in-network clinics by Progyny's Provider Relations team. Following an IVF transfer, providers are required to report outcomes of the transfer to Progyny within three months, reflecting the time clinically needed to confirm outcomes. According to Progyny, they have a 95% reporting rate for treatments at in-network providers, which is comparable to the CDC reporting rate. Out-of-network providers are not required to submit outcomes to Progyny and, therefore, are not included in the study. Out-of-network transfers represent a minimal portion of Progyny's total IVF transfers.

The national datasets used in Progyny's Fertility Outcomes Study include the SART 2019 National Summary Report and the CDC 2020 National Summary and Clinic Data Sets. Both of these data sets were made available in 2022 and were the most recent and complete datasets available at the time of Progyny's study. Nationally, over 440 clinic entities provide fertility services to patients. The CDC estimates that they collect data and report on more than 95% of all ART cycles in the United States.² SART completion rates are unknown.

Progyny also analyzes data from the CDC and SART at the fertility clinic level. This data was used to compare Progyny member outcomes to non-Progyny member outcomes across in-network clinics and out-of-network clinics in Progyny's Fertility Outcomes Study. While clinic level SART data is available publicly, Progyny purchases an export of the clinic level data in a single workbook. Progyny utilized a list of in-network clinics as of March 22, 2022. Progyny summarized the total volume in each measure for in-network clinics and then removed Progyny volume to calculate the in-network non-Progyny volume.

DATA PERIODS

The data provided by Progyny includes fertility services provided in 2021 and includes data runout through March 28, 2022. For the national average, non-Progyny in-network populations, and non-Progyny out-of-network populations, Progyny calculated the pregnancy rate per IVF transfer, IVF miscarriage rate, and SET rate comparisons using SART data from 2019, and calculated the IVF live birth rate and IVF multiples rate using CDC data from 2020. This is outlined in Table 2 below.

² <https://www.cdc.gov/art/nass/index.html>

Table 2
Progyny's Fertility Outcomes Study
Sources for External Data by Fertility Outcome

Measure	Source
Pregnancy Rate (per Transfer)	SART 2019 Final
Miscarriage Rate (per Pregnancy)	SART 2019 Final
Live Birth Rate (per Transfer)	CDC 2020 Preliminary
Single Embryo Transfer Rate (per Transfer)	SART 2019 Final
Multiples Rate (per Live Birth)	CDC 2020 Preliminary

These data sets are the most recent data available from SART and the CDC. The lag in SART and CDC data is due to the live-birth delivery data that requires data through October of the following year to account for the gestational period. Further data lags occur due to the time clinics need to report data to the CDC, and the time it takes the CDC to validate and analyze the data. However, even when Progyny data from the same time period is compared to SART and CDC data, differences between Progyny versus CDC and SART outcomes are directionally consistent and statistically significant.

It should be noted that the CDC, SART, and Progyny data used in this analysis may be impacted by the COVID-19 pandemic. The impact of COVID-19 on fertility outcomes is unclear, but there may be biological risks of COVID-19 that would affect fertility outcomes, as well as behavioral changes from members and fertility clinics.

POPULATION SELECTION AND NORMALIZATION

The Progyny fertility outcomes include IVF transfers from in-network providers only. Progyny compares fertility outcomes for Progyny members who received care from in-network providers to both the non-Progyny national datasets, non-Progyny members who received care from in-network providers, and non-Progyny members who received care from out-of-network providers. Progyny was unable to exclude members who may have used a donor egg, as they do not collect this information from their providers. Age was not provided for members who used a donor egg in the SART national dataset, and those members were, therefore, excluded from Progyny's analysis. Table 3 outlines the number of IVF transfers included in each dataset.

Table 3
Progyny's Fertility Outcomes Study
Number of IVF Transfers by Population

Population	Number of IVF Transfers
Progyny 2021	9,633
CDC 2020	110,024*
SART 2019**	134,377*

*These numbers include Progyny members.

**SART includes transfers that occurred more than a year after the retrieval, whereas the CDC does not.

Note, these IVF Transfers are a subset of ART cycles as reported by SART, CDC, and Progyny. Total cycles reported also include retrievals and egg freezing that are not pregnancy attempts.

The national averages are reported by the following age categories: <35, 35 to 37, 38 to 40, >40 for the CDC, and <35, 35 to 37, 38 to 40, 40 to 42, >42 for SART. As a result, Progyny categorizes treatment outcomes into these age categories depending on the age of the member at their service date.

Progyny accounts for differences in age between the Progyny population and the non-Progyny national population. Progyny re-weighted the benchmark data to match the age distribution of the Progyny population to enable age-adjusted comparisons to Progyny's outcomes. The age groups used by Progyny were aligned to those used in the CDC national data set.

FERTILITY OUTCOME MEASURES

The following methodology was used by Progyny to calculate each of the measures:

- **IVF Pregnancy Rate** = IVF Transfer with Clinical Pregnancy / IVF Transfer with Reported Pregnancy Outcomes
- **IVF Miscarriage Rate** = IVF Miscarriage / IVF Transfer with Clinical Pregnancy
- **IVF Live Birth Rate** = (IVF Transfer with Clinical Pregnancy – IVF Miscarriage) / IVF Transfer with Reported Pregnancy Outcomes
- **IVF Multiples Rate** = IVF Transfer with Multiples / IVF Transfer with Reported Fetal Heartbeats
- **SET Rate** = IVF Transfer where One Embryo was Transferred / IVF Transfer

These particular measures were chosen to measure pregnancy success, health of the pregnancy, and health of the baby. These are the most commonly reported measures to evaluate fertility outcomes. In our research, particularly when reviewing the CDC reports and datasets, we did not find any additional measures that would be used to measure these fertility outcomes. CDC has one of the most comprehensive fertility datasets in the U.S. For example, SET is used to avoid multiple-fetus pregnancies, which are associated with increased risk of poor health outcomes for mothers and infants. These poor health outcomes among infants include preterm birth, low birth weight, neurological impairments, and death.

III. REVIEW OF PROGNYN FERTILITY OUTCOMES STUDY COMPONENTS

In this section, we describe our interpretation of each component that was included in the development of the Progyny outcomes study results and provide our comments on the reasonableness of each component for measuring fertility outcomes. Additionally, we discuss other items that are currently not included, but may be appropriate to consider in the future. The items provided below are intended to be suggestions if Progyny performs future iterations of Progyny's Fertility Outcomes Study and are not shortcomings of the current methodology.

DATA PERIODS

Progyny's Fertility Outcomes Study compares 2021 Progyny outcomes to national outcomes from 2019 and 2020. While Progyny utilizes the latest data available from 2021, CDC and SART report data at a much larger lag. A refinement to this analysis could be to include Progyny fertility outcomes from time periods that align with the national data sets, which would also demonstrate changes over time. As Progyny uses more recent data than available from CDC and SART, any annual improvements in Progyny data may be contributing to the difference between Progyny and external populations. However, even when Progyny data from the same time period is compared to SART and CDC data, differences between Progyny versus CDC and SART outcomes are statistically significant and directionally consistent, as shown in Table 1 in the prior section.

HISTORICAL EXPERIENCE

We did not separately audit the historical experience provided to us by Progyny. We cannot comment on the accuracy of the data, including, but not limited to, underlying claims, completion factors, demographic/characteristic identification, or network status of clinics. Of the 10,147 reported IVF transfers for Progyny members, 9,633 (95%) included reported pregnancy outcomes. The only exclusions that Progyny made to their dataset was to exclude members who went to out-of-network providers for their fertility treatment. The data was not included because while Progyny members are allowed to continue treatment at an out-of-network providers due to transition of care, out-of-network providers are not required to provide data to Progyny. Based on our review of the size of each population included, we concluded that the internal and external populations are sufficiently credible for the Progyny Fertility Outcomes Study.

POPULATION SELECTION AND NORMALIZATION

As discussed in Section II above, Progyny's Fertility Outcomes Study methodology consisted of summarizing historical experience and applying national percentages to Progyny's member volume in each age band to normalize for differences in age between internal and external groups. The age-adjusted value for the external population is compared to that for the internal group to estimate the difference in clinical fertility outcomes. The authors of this report found Progyny's methodology for age-adjusting the external population to be reasonable.

While Progyny normalized the data for difference in age, there may be other patient characteristics that may contribute to differences in fertility outcomes that are not reported in the comparator CDC and SART data sets by age. Other factors that may contribute to differences in fertility outcomes include infertility diagnosis, which may include diminished ovarian reserve, endometriosis, male factor, uterine factor, tubal factor, ovulatory dysfunction, or unexplained infertility. While the CDC collects this data, they do not report it by different age brackets, limiting the ability to compare outcomes data on these variables. Progyny data includes patients who used a donor egg, while donor egg cycles are excluded from the CDC and SART data. The CDC and SART data does not report on donor egg cycles by age group. There may be a difference between members who used their own egg versus a donor egg, especially in the >40 age group, as older members using an egg from a younger donor may result in difference in clinical outcomes. According to the CDC, older patients are more likely to have a live birth when a donor egg is used, compared to when they use their own egg, as donors are typically in their 20s or early 30s and do not experience infertility.³ Additionally, the Progyny dataset is comprised of members who have fertility benefit coverage through their employer, while the external populations include a mixture of employer-funded and self-pay members. Due to the large expense associated with IVF, self-pay members may have financial considerations that Progyny members may not have. These financial considerations may influence member decision making that could impact clinical fertility outcomes. Self-pay members may be more likely to transfer multiple embryos and /or forego PGT, an additional service provided during an IVF cycle used to detect chromosomal or genetic abnormalities. The percentage of IVF transfers of at least one embryo with PGT

³ <https://www.cdc.gov/art/pdf/2016-report/ART-2016-National-Summary-Report.pdf>

was 43.8% in the 2019 CDC data set. As Progyny covers PGT, it may lead to higher SET rates in the Progyny population.

Progyny and the CDC both achieve a 95% reporting rate. It is unknown what effect inclusion of the clinics that did not report outcomes would have on the fertility measures included in the Progyny study.

FERTILITY OUTCOME MEASURES

We confirmed the measures used in the Progyny Fertility Outcomes Study are appropriate, and commonly used measures to summarize fertility data. We consider the five measures studied by Progyny to be sufficient to measure the efficacy of a fertility program. These measures are commonly used in the literature to measure pregnancy success, health of the pregnancy, and health of the baby.

Progyny's current IVF live birth rate is calculated by subtracting the IVF miscarriage rate from the IVF pregnancy rate, while the national benchmarks are based on actual reported live birth rates. In addition to clinical documentation of a miscarriage, if a member received a subsequent ART treatment, Progyny assumes the member's prior IVF cycle did not result in a live birth. Progyny's live birth rate calculation may be impacted by miscarriage data and may be overstated if miscarriages are under-reported. This is particularly important for IVF cycles that occurred in the fourth quarter of 2021, as Progyny data would only capture miscarriages through March 28, 2022. However, the chance of having a miscarriage after 13 weeks is 1.3% and unlikely to impact the miscarriage rate significantly.⁴

In the 2019 SART data, the embryo transfers are split out into initial embryo transfer and subsequent embryo transfer. While the number of transfers is provided for the initial embryo transfer group, it is not available for the subsequent embryo transfer group. As a proxy, Progyny utilizes the number of thaw procedures to estimate the number of transfers in the subsequent embryo transfer group and appropriately removes thaws with no suitable embryo for transfer. It is possible that some of these thaw procedures were intended for use in a gestational carrier, thus, would not be used in a Progyny member. However, transfers of intended parent tissue into gestational carriers only account for 2.7% of all patient embryo transfers in the 2019 SART data, so it is unlikely to make a directional change in the results.

⁴<https://datayze.com/miscarriage-chart>

IV. CONCLUSION

In general, Milliman actuaries consider Progyny's methodology to be appropriate and reasonable to estimate clinical outcome differences between Progyny's population, the non-Progyny national population, the non-Progyny in-network population, and the non-Progyny out-of-network population. We focused our review on the overall methodology and calculation of the clinical outcomes used in the Progyny Fertility Outcomes Study. During our review of the Progyny's Fertility Outcomes Study methodology, we identified some factors which may account for differences between the Progyny and external populations, such as differences in time periods, infertility diagnosis and IVF cycle characteristics. While the CDC collects data on infertility diagnosis and IVF cycle characteristics, they do not report it by different age brackets, limiting the ability to compare outcomes data on these variables. Additionally, with respect to the differences in time periods, even when Progyny data from the same time period is compared to SART and CDC data, differences between Progyny versus CDC and SART outcomes are statistically significant and directionally consistent. The results from the Progyny Fertility Outcomes Study may not be representative of an individual member's specific experience. Analyzing the drivers of Progyny's clinical outcomes with respect to their product offering was not within the scope of this analysis.

V. DATA RELIANCE AND IMPORTANT CAVEATS

Jason B. Gomberg, Erica Reijula, and Hiram Satterwhite are consulting actuaries with the firm of Milliman, Inc., members of the American Academy of Actuaries, and meet the Qualification Standards of the Academy to render the actuarial opinion contained herein. To the best of our knowledge and belief, this report is complete and accurate and has been prepared in accordance with generally recognized and accepted actuarial principles and practices.

This report should be reviewed in its entirety. The information in this report is intended for use of Progyny to provide third-party validation of Progyny's calculation of clinical fertility outcomes and methodology. It may not be appropriate and should not be used for other purposes. This work has been prepared for Progyny to share with third party stakeholders. We do not intend this information to benefit, or create a legal liability to, any third party, even if we permit the distribution of our work product to such third party. The information in this report is qualitative in nature, and no party should rely on this information without requiring a thorough review and understanding of assumptions, methodology of the Progyny Fertility Outcomes Study itself, and extensive knowledge of fertility clinical outcomes.

Our assessment is formed based on information made available to us by Progyny. We accepted this information without audit but reviewed the information for general reasonability and consistency. If the underlying data or information is inaccurate or incomplete, the contents of this report along with many of our conclusions, may likewise be inaccurate or incomplete. If there are material defects in the data and information, it is possible they would be uncovered by a detailed, systematic review and comparison of the data to search for questionable data values or for relationships that are materially inconsistent. Such a review is beyond the scope of this assignment.

The terms of Milliman's Master Services Agreement with Progyny effective March 27, 2019, apply to this report and its use.

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