

SYSTEMATIC REVIEW

Incidence and Comparison of Suicide in Various Phases of the Menstrual Cycle: a Systematic Review and Meta-analysis

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ABSTRACT

Background: Suicide is a global health concern. There are reproductive health-related factors that are responsible for increasing the risk of female suicide. There are a number of studies examining the association between suicide and the menstrual cycle, but still, there are no conclusive findings. **Aim:** We aimed to pool data from all the studies reporting data on suicides and the menstrual cycle phase to report the following outcomes: incidence of suicidal deaths in the menstrual, secretory, and proliferative phases, and to find out whether the burden of suicide in the menstrual phase in particular, was more at a young age (18-35 years) or middle age (36-50 years). **Methods:** The PubMed database was extensively searched from inception till 12th April 2022. The data for the number of events occurring for each outcome were pooled using random-effects model and forest plots were created. **Results:** Five articles were shortlisted for inclusion in our analysis. Incidence of suicide in the secretory phase was highest at 45.2% [95% CI, 0.367–0.537]. The incidence of suicide, when occurring in the menstrual phase, was reported to be 68.4% (95 CI, 0.317–1.052) and 31.6% (95 CI, -0.052.3–0.68) for young-aged and middle-aged victims, respectively. **Conclusion:** Our results demonstrate that the menstrual phase has a lower risk of mortality due to suicide when compared to the other two phases of the menstrual cycle. Nevertheless, when suicide occurred in the menstrual phase, the incidence of suicide among the younger age-group was higher than for those in the middle age-group.

Key words: Women's health issues, Menstruation; Suicide, Uterine histopathology

1. INTRODUCTION

Suicide is a global public health concern. Every year, around one million people die by suicide, 10–20 million people attempt suicide, and 50–120 million individuals are profoundly impacted by the suicide or attempt of a close friend or family member (1). In 1998, suicides constituted 1.8% of the global illness burden; by 2020, this proportion was projected to rise to 2.4% (2). Despite the expanding body of information and research on suicidal behavior, its interpretation and integration are challenging because of the numerous presentations that will invariably be a part along the spectrum of suicide. Among the traits usually assessed are suicidal ideation, which is described as “contemplation about one's own death”, and suicide attempt, which is defined as “self-injurious behavior

with the implied or explicit aim to die” (3). Co-occurring mental disorders that exacerbate distress (such as panic disorder or post-traumatic stress disorder) or lessen constraint (such as drug misuse or cluster B personality disorders) accelerate the shift from suicidal ideation to suicide attempt (4). Among women, additional factors such as menstrual cycle, postpartum psychosis, pregnancy, abortion, and marriage related issues also serve as stressors for female suicide (5).

The frequency of suicidal attempts varies between males and females, which can be related to the possible association of suicidal behavior with factors such as the menstrual cycle and gonadal hormones (6). The menstrual cycle, which is defined as the monthly set of changes that a woman's body undergoes, consists of four dis-

tinct phases: the menstrual phase, follicular phase, ovulatory phase, and luteal phase; and these are influenced by various female hormones (7). However, they can also be simplified and categorized as the menstrual phase, the secretory phase, and the proliferative phase. The advantage of using 3 phases is that the length of the phases is similar. This similarity in the length of the phases removes the inherent risk during assessment, that, a phase that lasts longer will always mathematically have more suicides. Variation in the levels of these hormones during the different phases alters the level of dopamine, which influences mood and suicidal behavior (8).

As per our literature search, there are a number of studies examining the association between suicide and the menstrual cycle in relation to suicide attempts and fatalities. Several disparities exist in the results. In one study, researchers examined the association between menstruation and suicide attempts in 76 individuals who self-poisoned or self-injured themselves. The study found no relation between menstruation and suicidal attempts (9). In contrast to those findings, several other studies have shown a correlation between suicide, suicidal thoughts, and menstrual cycle phase (10,11). The literature show inconsistency in the results, with no clear agreement on whether there is a correlation between the menstrual cycle stages and suicide.

2. AIM

We aimed to pool data from all the studies reporting data on suicides and the phase of the menstrual cycle to see if collated findings could be useful in assessing if the incidence of suicide is greater in any particular phase of the menstrual cycle. It was also hoped that our findings could also assist suicide prevention programs in developing more effective strategies to reduce the suicide rate.

3. METHODS

This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards (12,13).

Data sources and search strategy

PubMed database was extensively searched from inception till 12th April, 2022. The detailed search strategy is provided in **Supporting Information Table S1**. Selected articles were transferred to Endnote X7 (Clarivate Analytics, PA), to check and remove duplicates. Two reviewers independently reviewed the relevant articles. Any discrepancies were rectified by a senior reviewer. Initial search was completed by reading titles and abstract after which the shortlisted articles were assessed for full text.

Study selection

Studies were considered for the meta-analysis if they met the following inclusion criteria: [1] studies were autopsy reports or retrospective cohort studies; [2] if they contained following outcome: fatal suicide attempt, where the study indicated that the suicide resulted in immediate death of the individual, in the menstrual, secretory, and luteal phases; [3] were published in English or had abstracts which were translated to English and sufficiently reported our outcomes of interest in the translated abstract. Case reports, editorials, clinical trials, narrative reviews, systematic reviews and meta-analysis were excluded. Those studies which reported data on fatal suicide

attempts without mentioning the specific phase of the menstrual cycle were excluded as well.

Data extraction

Two reviewers independently extracted data on essential baseline characteristics of the included studies. Our outcomes of interest were following: suicidal deaths in menstrual phase, suicidal deaths in proliferative phase, suicidal deaths in secretory phase, and suicidal deaths at young age during menstrual phase and suicidal deaths at middle age during menstrual phase.

Statistical analysis

The statistical analysis was performed using OpenMeta-Analyst (14). The prevalence of suicidal deaths in a particular phase was calculated by dividing deaths in that phase with total number of deaths in all the phases of menstrual cycle and frequencies were calculated. Then for all other outcomes, percentage was obtained by dividing the incidence of a particular outcome by the total number of suicidal deaths which occurred during the menstrual cycle. A meta-analysis was conducted on the calculated frequencies of the outcomes of interest and an average incidence was obtained for each outcome, along with confidence intervals (CI). Further, we evaluated the odds ratio (OR) for mortality for completed suicides in menstrual phase against other phases. I^2 was used to assess the heterogeneity between the studies and a value of $I^2 = 25\%–50\%$ was considered mild, $50\%–75\%$ as moderate, and $> 75\%$ as severe (15). A p-value of < 0.05 was considered significant in all cases. The quality assessment for each included study in the meta-analysis was performed using the Newcastle–Ottawa Scale (16).

4. RESULTS

Literature search and study characteristics

Our initial search yielded 707 articles. After title and abstract screening, 667 articles were removed. Further evaluation of full-text of the remaining 40 articles resulted in exclusion of 35 articles. Five studies were included in our meta-analysis. The results of the study selection process are summarized in **Figure 1 (PRISMA flowchart)** Figure 1 summarizes the findings of the study selection procedure.

The baseline characteristics of the 5 included (17–21) studies are summarized in **Table 1**. A total of 425 individuals were included in the study. The range of reproductive age for women was reported to be 11–50 years. Since only five studies were included, publication bias was not assessed by using funnel plots. The results of quality assessment are given in **Supplementary Table 1**.

Results of meta-analysis

Summarized results of the meta-analysis are presented in **Figure 2**. The forest plots are given in **Supplementary Figure S1–S5**.

Suicide deaths in the menstrual phase: All five selected studies reported the incidence of deaths due to suicide in the menstrual phase (total deaths, 425; events, 81). Pooled analysis demonstrated a 17.5% [95% CI, 0.072–0.278] incidence of suicide in the menstrual phase. The findings are summarized in **Figure S1**.

Suicide deaths in the secretory phase: All 5 selected articles reported results on deaths due to suicide in the secretory phase of the cycle (total deaths, 425; events, 199). Pooled analysis

Study name	Country	Age (Range)	Total sample	Number of deaths due to suicide	Time duration	Type of study
Vanezis et al. 1990	United Kingdom	11-50 years	257	50	1982–1989	Retrospective
Balaram et al. 2018	India	15-45 years	95	95	2004-2005	Retrospective
Behera et al. 2019	India	12-48 years	547	86	2 years	Retrospective
Jeevagan et al. 2020	India	15-45 years	150	150	2018-2019	Retrospective
DSouza et al. 2017	India	11-48 years	44	44	2010-2011	Retrospective

Table 1. Baseline characteristics of the studies

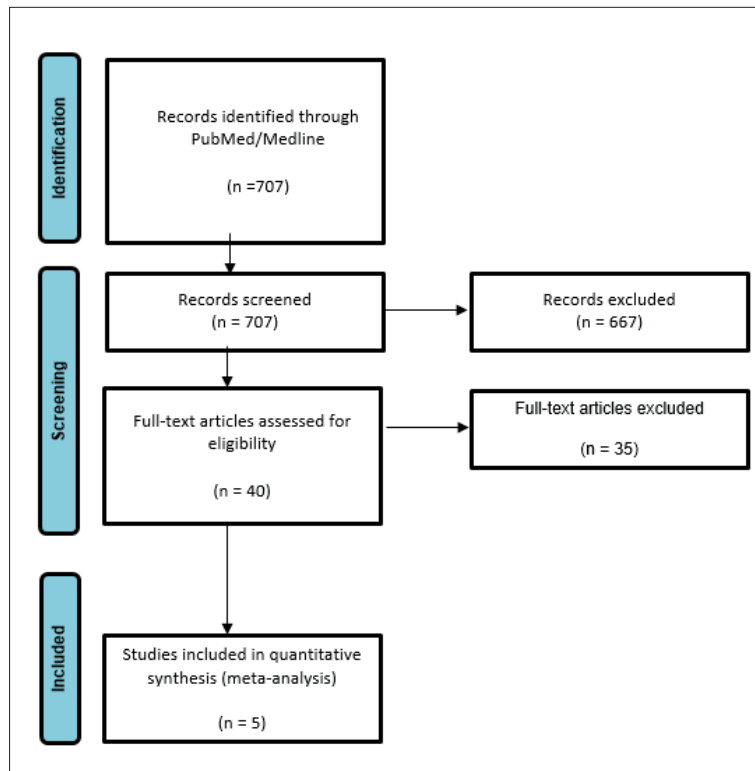


Figure 1. PRISMA flowchart

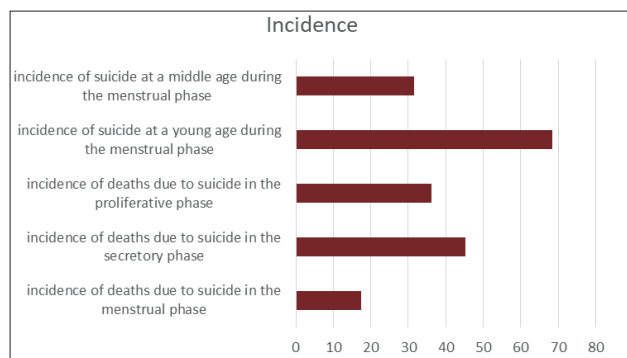


Figure 2. Summary of the results of the meta-analysis

shows a 45.2% (95% CI, 0.367–0.537; **Figure S2**) incidence of suicide in the secretory phase of the monthly cycle.

Suicide deaths in the proliferative phase: All 5 selected studies reported on deaths that occurred during the proliferative phase due to suicide (total deaths, 425; events, 142). Our pooled analysis demonstrated a 36.2% (95% CI, 9.4–25.1; **Figure S3**) incidence of suicide in the proliferative phase of the menstrual cycle.

Suicide deaths in the menstrual phase at young age (18-35 years): Out of 5 selected studies, 2 reports reported on deaths that occurred during the menstrual phase at a young age (total

deaths, 13; events, 8). Our pooled analysis demonstrated a 68.4% (95% CI, 0.317–1.052; **Figure S4**) incidence of suicide at a young age during the menstrual phase.

Suicide deaths in the menstrual phase at middle age (36-55 years): Out of 5 selected studies, 2 reports reported on deaths that occurred during the menstrual phase at middle age (total deaths, 13; events, 5). Our pooled analysis demonstrated a 31.6% (95% CI, -0.052.3–0.68; **Figure S5**) incidence of suicide at middle age during the menstrual phase.

Odds ratio for suicide deaths in the menstrual phase versus other phases: All 5 studies reported data on suicide during the menstrual, secretory, and proliferative phases. Our analysis demonstrates that the risk of suicide was higher in the secretory phase (RR: 0.41; 95% CI, 0.33 – 0.51, p-value < 0.00001; **Figure S6**) and proliferative phase (RR: 0.57; 95% CI, 0.45 – 0.73, p-value < 0.00001; **Figure S7**).

5. DISCUSSION

Our study reports on the incidence of suicidal deaths in particular phases of the female reproductive cycle, namely the menstrual, proliferative, and secretory phases. The results obtained demonstrate that the menstrual phase has a lower risk of mortality than the other two phases of the menstrual cycle. We also categorized deaths in the menstrual phase based on the victim belonging to either the young age-group or middle age-group. To the best of our knowledge, our meta-analysis is the first study to focus solely on these outcomes.

This analysis shows that suicidal deaths were more common in the secretory phase of the menstrual cycle as compared to the menstrual and proliferative phases. This finding is in accordance with another study in which the majority of the suicidal deaths occurred during the secretory phase (19). Similarly, in another study in which a comparison was made between non-suicidal deaths and suicidal deaths, the incidence was higher in the secretory phase than in the menstrual phase (20). In contrast to the aforementioned studies, there are some studies in which opposite findings were reported. In one study, which was conducted in India, most of the deaths occurred in the proliferative phase (18), whereas in another study, most of the fatalities were menstruating at the time of the fatal suicide attempt (10). The disparities in results could be due to differences in methodology; a shift in the emphasis of concern from fatal suicide attempts to non-fatal suicide attempts; and varying definitions in relation to terminology, which might all contribute to the difficulty in reaching a conclusion.

Hypo-estrogenic status throughout secretory and men-

strual phases may explain why there are more suicide fatalities during the secretory and menstrual phases than during the proliferative phase (22). Estrogen promotes dopaminergic activity in the brain through increased dopamine receptors in humans, therefore a drop in estrogen hormone results in a fall in dopamine levels, which can lead to suicidal ideation (23,24). Serotonin may play a role in suicide risk, particularly in at-risk individuals. The menstrual cycle has an impact on serotonin function. As a neuromodulator, estrogen is extremely essential (25). Estrogen binds to intracellular receptors, allowing for the production and metabolism of neuropeptides, neurotransmitters and their receptors, nerve growth factors, neurotransmitter transporters, and signal transduction proteins (26). Estrogen improves 5-hydroxytryptamine (5-HT) activity by raising the concentration of 5-HT receptors (27). Suicide risk in women with predisposing characteristics is increased by low serotonin levels produced by reduced estrogen hormone (28).

Our study also reported the incidence of suicidal deaths in the menstrual phase of women's monthly cycle at young age, 18 to 35 years, and middle age, 36 to 55 years, categories based on a previous study (29), however, none of the included participants were above 50 years of age. The findings here indicate that suicidal death, when occurring during the menstrual phase, was higher among the younger aged victims than those at middle age, whereas previous studies reported that suicidal deaths were more common at age 26–30 years, but no specific phase was mentioned (19). Age is a major predisposing factor, and it is also linked to other factors such as the female's occupation and socioeconomic position, making it vital to further investigate.

We offer the most recent statistics on the occurrence of suicide fatalities throughout the menstrual, secretory, and proliferative phases of the female reproductive cycle. Our findings contradict prior meta-analyses in which fatal suicide was an outcome; in that study, the majority of the individuals were menstruating during the fatal suicide event (30). Histopathological investigation was used to determine the appropriate phase of the monthly cycle. In our study, the majority of individuals were between the ages of 15 and 49, when the female reproductive cycle is most likely to occur. It is hoped that these findings could also assist suicide prevention programs in developing more effective strategies to reduce the suicide rate based on possible hormonal intervention strategies.

There were several limitations to our study. Firstly, the sample size was very small. Secondly, most of the studies were from India, which can cause the generalization of our results to a specific population as there are multiple region-specific factors that may play an additional role in both fatal and non-fatal suicide attempts. Thirdly, there are various factors that may contribute to an increase in suicidal deaths, factors that work in conjunction with menstrual cycle changes; those factors were not assessed in this study. Though this study ana-

lyzed incidence patterns of suicides based on the phase of the menstrual cycle, the base articles used were in some instances proof of concept or rather starting points to see if further research on this line of research was worth looking into. Based on our analysis, the numbers show that a link is present in terms of the frequency of suicides and the phase of the menstrual cycle where it is most likely to occur. But a multi-pronged research approach in future studies is needed in order to conclusively prove the possible pathophysiology behind it. We recommend that future studies on female suicidology and the menstrual cycle incorporate hormonal analysis (specifically estrogen and progesterone) with psychiatric or psychological assessments of high-risk women (for example women suffering from depression) at the very least. Though dopamine blood levels are not an accurate indicator of dopamine efficacy at the neuronal level, there might still be some merit if studies could incorporate it as well. In addition, levels of serotonin are known to vary in at-risk individuals for suicide (31). Estimation of its levels and comparison with gonadal hormone levels is another avenue that should be concentrated on. The value of histopathological studies, in cases of suicides, then comes to conclusively establish the menstrual cycle phase. In any case, more robust studies are required from different regions of the world with a larger sample size to further corroborate these results. Based on our recommendations for future research, we hope those studies will help mitigate the inconsistencies of the results that persist in studies concerning the role of the menstrual cycle in both fatal and non-fatal suicide attempts.

6. CONCLUSION

This study shows that the incidence of suicide was lower in the menstrual phase as compared to the secretory or proliferative phases, both of which had significantly higher risk of mortality. Our findings also demonstrate that suicide, when occurring during the menstrual phase, was more prevalent among younger aged females than middle aged.

- **Patient Consent Form:** Not available.
- **Authors contribution:** YAA: Conceptualization; Participated in literature search; methodology; drafting the paper. AMR: Methodology; formal analysis; drafting the paper. SSJ: Methodology; formal analysis; drafting the paper. MAK: Participated in literature search; methodology; drafting the paper. MA: Conceptualization; methodology; revision of the paper. HLD: Conceptualization; methodology; revision of the paper. AA: Conceptualization; methodology; revision of the paper. RGM: Conceptualization; methodology; revision of the paper. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
- **Conflict of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** Nil.

Online supplementary information

Pubmed: (((("menstrually"[All Fields] OR "menstruation"[MeSH Terms] OR "menstruation"[All Fields] OR "menstrual"[All Fields]) AND ("phase"[All Fields] OR "phase s"[All Fields] OR "phases"[All Fields])) OR ("mense"[All Fields] OR "menstruation"[MeSH Terms] OR "menstruation"[All Fields] OR "menses"[All Fields]) OR ("menstrual cycle"[MeSH Terms] OR ("menstrual"[All Fields] AND "cycle"[All Fields]) OR "menstrual cycle"[All Fields])) AND (((("immediate"[All Fields] OR "immediately"[All Fields]) AND ("death"[MeSH Terms] OR "death"[All Fields] OR "deaths"[All Fields])) OR ("death"[MeSH Terms] OR "death"[All Fields] OR "deaths"[All Fields]) OR ("suicide, completed"[MeSH Terms] OR ("suicide"[All Fields] AND "completed"[All Fields]) OR "completed suicide"[All Fields] OR ("completed"[All Fields] AND "suicide"[All Fields])))

Number of results: 707

Supplementary Table S1. Search string used for data extraction from inception till 12th April, 2022

	Selection		Comparability		Outcome		Score	
Study name	Representativeness of the exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	(quality)
Vanezis et al. 1990	*	*		*	*	*	*	Fair
Balaram et al. 2018	*	*		*	*	*	*	Fair
Behera et al. 2019	*	*		*	*	*	*	Fair
D'Souz et al. 2017	*	*		*	*	*	*	Fair
Jeevagan et al. 2020	*	*		*	*	*	*	Fair

Supplementary Table S2. Quality assessment

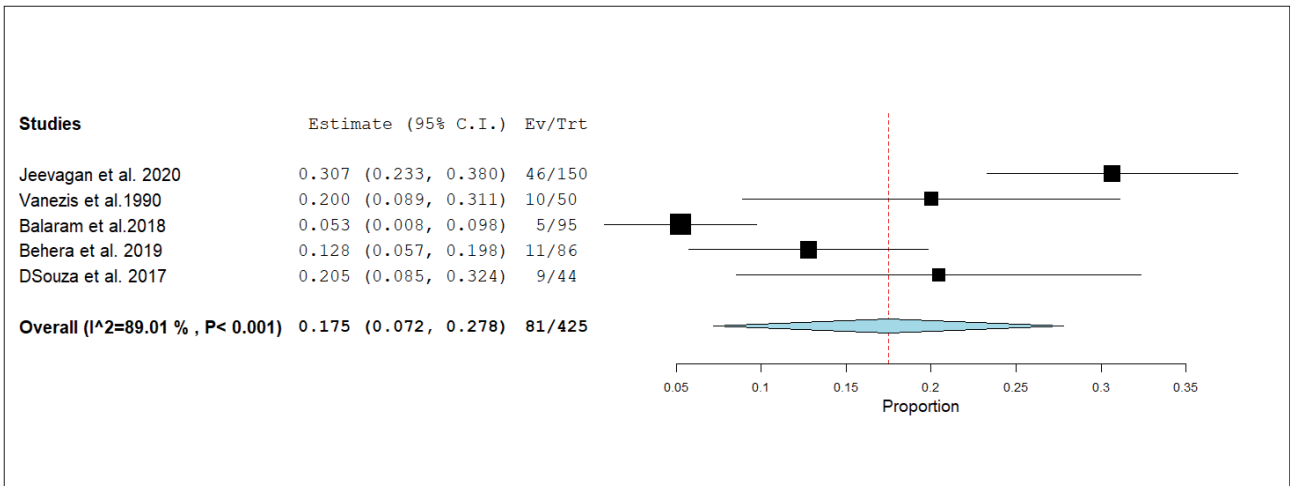


Figure S1. The incidence of deaths due to suicide in the menstrual phase

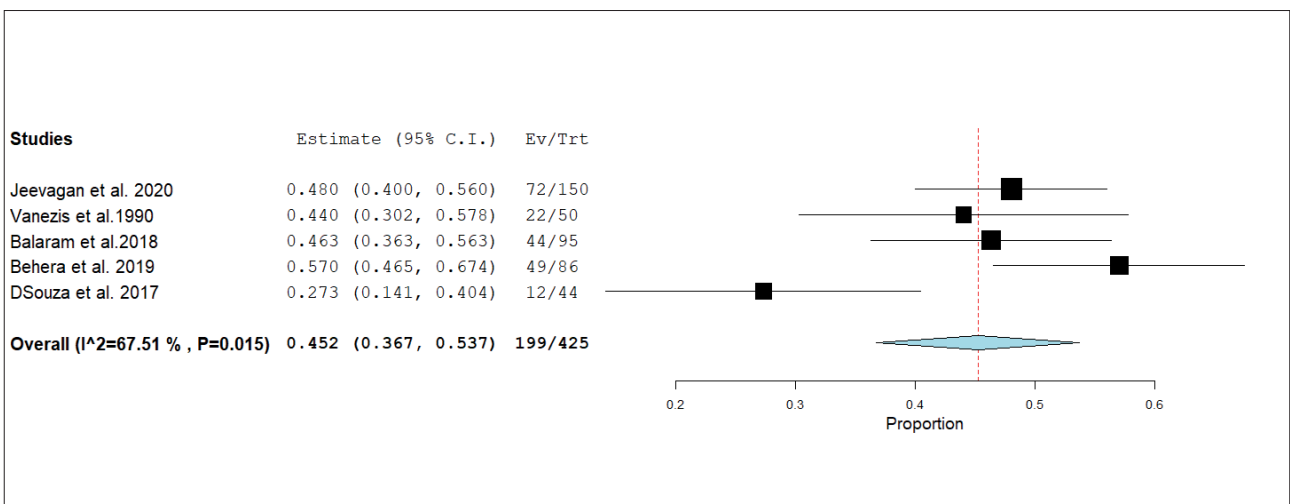


Figure S2. The incidence of deaths due to suicide in the secretory phase

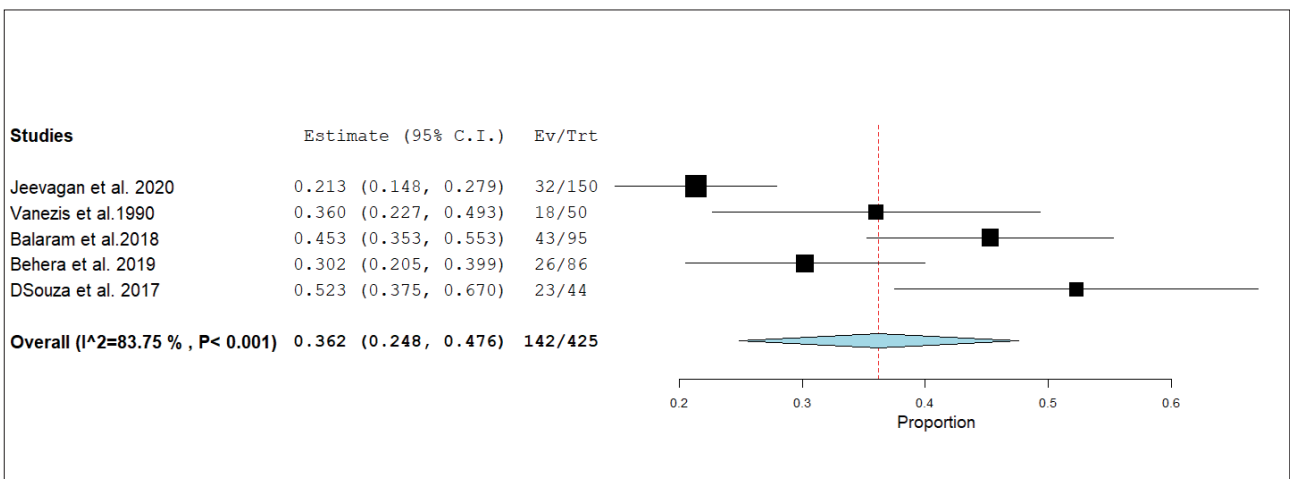


Figure S3. The incidence of deaths due to suicide in the proliferative phase

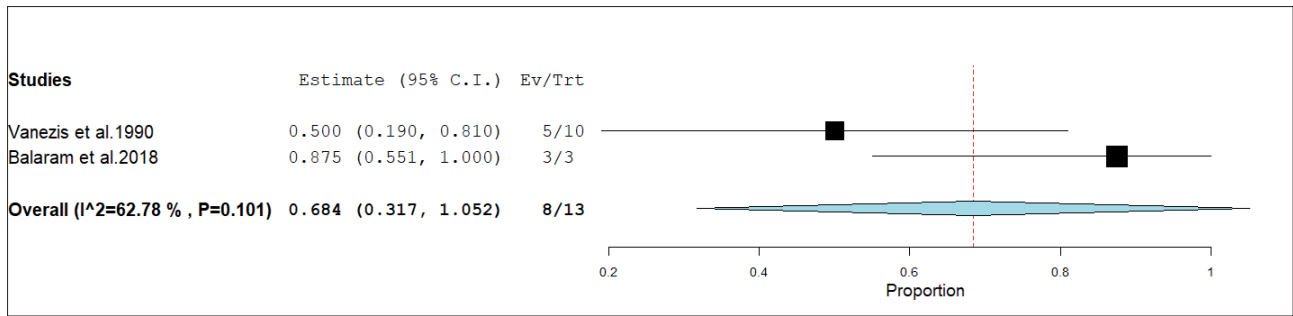


Figure S4. The incidence of suicide at a young age during the menstrual phase

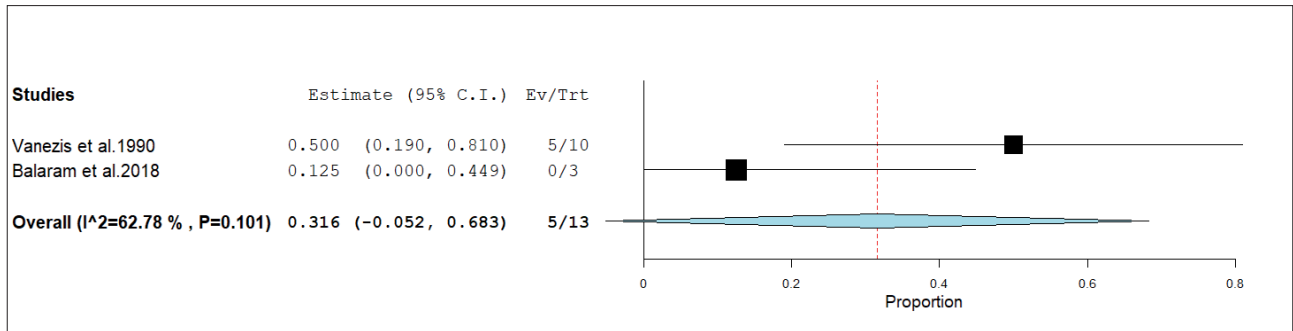


Figure S5. The incidence of suicide at a middle age during the menstrual phase

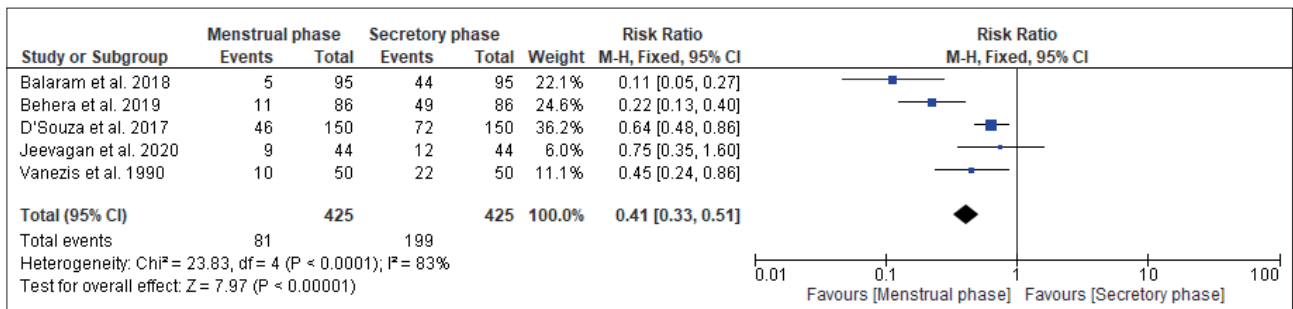


Figure S6. Forest plot showing risk ratio of death between menstrual phase and secretory phase

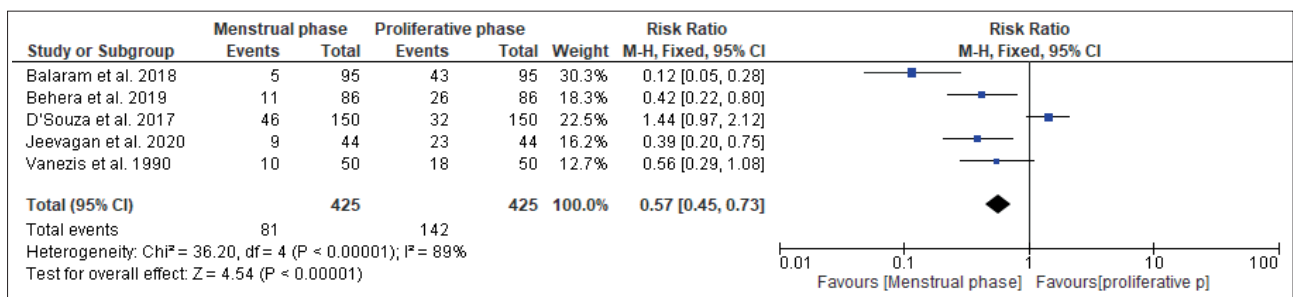


Figure S7. Forest plot showing risk ratio of death between menstrual phase and proliferative phase

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