

Annotated bibliography of studies in the meta-analysis

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1. Subak LL, Adamson GD, Boltz NL. Therapeutic donor insemination: A prospective randomized trial of fresh versus frozen semen. *Am J Obstet Gynecol* 1992;166:1597-1606.
 - This is a randomized clinical trial (RCT) lasting 6 cycles. Randomization was by a random number table with discarding of those sequences with strings of 3 consecutive cycles of same treatment. This is the only study in which the method of randomization was specified. Fresh and frozen cycles used the same donor (5 exceptions). Minimum criteria for fresh semen were total count > 60 million/ml (CT = 60), total motility > 60% (MT=60), progressive motility > 30% (PMT = 30).
 - There is a graph but no table of life table data. The raw data, however, is available to E.J.L. For the meta-analysis, data of table I was used to calculate cycle fecundity.
 - There were 15 repeat courses (72 courses in 57 women). A better design would be to restrict analysis to the first treatment or to stratify in the analysis.

2. Iddenden DA, Sallam HN, Collins WP. A prospective randomized study comparing fresh semen and cryopreserved semen for artificial insemination by donor. *Int J Fertil* 1985;30:50, 55-6
 - This is a randomized clinical trial in which all cases were severe male factor infertility, CT < 1 million/ml. Minimum criteria for fresh semen were CT = 60, MT=60, Normal morphology > 60%. A constant volume of 1 ml was used for both fresh and thawed.
 - Data of Tables I and II were used to prepare a life table from which cycle fecundity was calculated.

3. Keel BA, Webster BW. Semen analysis data from fresh and cryopreserved donor ejaculates: comparison of cryoprotectants and pregnancy rates. *Fertil Steril* 1989;52:100-5.
 - This is a randomized clinical trial with randomization at each cycle. Used a constant volume, 2 ml (minimum CT = 20). There were 55 donors.
 - Data of Table 4 used to calculate cycle fecundity. No life table data. Used Mantel & Byer method (cites Olive D. *Fertil Steril* 1986;45:157). This is appropriate when subjects transfer to other group after spending some time in the first group (transplantation after being on waiting list, adoption, medical and surgical therapy for endometriosis).
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4. Brown CA, Boone WR, Shapiro SS. Improved cyropreserved semen fecundability in an alternating fresh-frozen artificial insemination program. *Fertil Steril* 1988;50:825-7
 - The first cycle was randomized and subsequent cycles alternated between fresh and frozen. Cross over designs in which pregnancy is the outcome are especially controversial.

- Totals from Table 1 were used for estimating the cycle fecundity for meta-analysis. The values in Table 1 do not compute correctly for a life table when summed from bottom up.
5. Richter M, Haning RV, Shapiro SS. Artificial donor insemination: fresh versus frozen semen; the patient as her own control. *Fertil Steril* 1984;41:277-80
 - The first cycle was randomized and subsequent cycles alternated between fresh and frozen. Cross over designs in which pregnancy is the outcome are especially controversial.
 - This is an earlier study by the same group of investigators as in Brown, above. The time is from 1976 to 1982 and the minimum criteria are less stringent: CT=60, MT=60, post thaw motility > 50% of initial motility.
 6. Smith KD, Rodriguez-Rigau, Steinberger E. The influence of ovulatory dysfunction and timing of insemination on the success of artificial insemination donor (AID) with fresh or cryopreserved semen. *Fertil Steril* 1981;36:496-502.
 - We used data of Table 4 to calculate cycle fecundity.
 - Data in Table 1 does not compute correctly from bottom up.
 - Assignment to fresh or frozen was dependent on availability of fresh donor.
 7. Schoysman-Deboeck A, Schoysman R. Clinical comparison of fresh and frozen semen. Page 295-300 in David G and Price WS editors, Human Artificial Insemination and Semen Preparation. Plenum Press, 1980 **AND** Schoysman-Deboeck A, Merckx M, Segal L, Vekemans M, Verhoeven N. Results of AID in 865 Couples, *Ibid*, Page 231-47.
 - Data on clinical factors listed in our table are from the second citation. We used data of Table 2 in the first citation to construct a life table limited to 12 months from which we calculated cycle fecundity.
 - Fresh semen was used whenever possible and frozen used if there was no fresh semen available.
 - Minimum criteria for fresh semen were CT = 80, MT=70. Post thaw CT and MT were about half that of fresh.
 8. Bordson BL, Ricci E, Dickey RP, Dunaway H, Taylor SN, Curole DN. Comparison of fecundability with fresh and frozen semen in therapeutic donor insemination. *Fertil Steril* 1986;46:466-9
 - We used data in Table 2, excluding cycles in which both fresh and frozen were employed, to calculate cycle fecundity. Numbers in Table 1 do not compute correctly when calculated from the bottom up.
 - Minimum criteria for fresh semen were CT = 60, MT=60. For post-thaw CT=40, MT=30 (Motile count = 12)
 9. Jackson MCN, Richardson DW. The use of fresh and frozen semen in human artificial insemination. *J Biosoc Sci* 1977;9:251-62.
 - We used data of Table 1 to calculate cycle fecundity.

- This study covers a 40 year period. Tubal patency was determined after 3-4 failed cycles.
10. Chong AP. Artificial insemination and sperm banking: clinical and laboratory considerations. *Seminars Reprod Endocr* 1985;3:193-200.
- We used data from Tables 6 and 7 used to construct life tables for calculating cycle fecundity.
11. Kossoy LR, Hill GA, Herbert GM, Parker RA, Rogers BJ, Daghli CS, Hebert CM, Wentz AC. Luteinizing hormone and ovulation timing in a therapeutic donor insemination program using frozen semen. *Am J Obstet Gynecol* 1989;160:1169-72
AND Kossoy LR, Hill GA, Herbert GM, Brodie BL, Daghli CS, Dupont WD, Wentz AC. Therapeutic donor insemination: the impact of insemination timing with the aid of a urinary luteinizing hormone immunoassay. *Fertil Steril* 1988;49:1026.
- This pair of papers covers the period 1984-1987 for fresh and 1987-88 for frozen.
 - Minimum criteria for fresh semen were CT = 80, MT=60, Normal morphology > 60%. For frozen semen the pre-freeze motility was >70%. A hysterosalpingogram was done after 3 failed cycles and laparoscopy after 6.
 - We combined data from LH and BBT monitoring groups (from Table 1 of first paper and Table 2 of second paper) and constructed 6 cycle life tables from which we calculated cycle fecundity.
12. DiMarzo SJ, Huang J, Kennedy JF, Villanueva B, Hebert SA, Young PE . Pregnancy rates with fresh versus computer-controlled cryopreserved semen for artificial insemination by donor in a private practice setting. *Am J Obstet Gynecol* 1990;162:1483-90.
- We used data of Table II to construct the life tables from which cycle fecundity was calculated. Cycles beyond the 10th were omitted.
 - Fresh was used from 1970 to 1987, usually with 2 inseminations; frozen from 1988-90, usually with better timed single insemination. Women who were having inseminations at the time of the switch to frozen were included only in the fresh group.
 - More women using frozen were over 35 years old, 46%, than women using fresh, 22%.
 - Data included 153 repeat fresh treatments and 2 repeat frozen treatments, presumably after a pregnancy. A treatment could include multiple insemination cycles. A better design would be to restrict analysis to the first treatment or to stratify in the analysis.
13. Bartlet EM, Penney LL. Therapeutic donor insemination: fresh versus frozen. *Missouri Medicine* 1994;91:85-88.
- We used data in Table 1 (number of cycles) and in the Results section text (number of pregnancies) to calculate cycle fecundity

- Fresh semen was used in 1985-88 and frozen in 1988-91. LH monitoring was used predominantly in the latter period. Laparoscopy was done after 6 failed cycles.
- There are duplicate treatments in both fresh (18 pregnancies among 15 women) and frozen (32 pregnancies among 27 women). A treatment could include multiple insemination cycles. A better design would be to restrict analysis to the first treatment or to stratify in the analysis.
- Table 4 cites pregnancy rates with frozen semen for 3 studies (Albrecht, Aiman, and Glezerman) that report only fresh semen results.

14. Leeton J, Selwood T, Trounson A, Wood C. Artificial donor insemination: frozen versus fresh semen. *Aust NZ J Obstet Gynaec.* 1980;20:205

- We used data of Table 2, combining early and late experience with frozen to compute cycle fecundity. Data in Table 1, life tables, does not compute correctly from bottom up. Authors used a modified life table method that did not include subjects who had withdrawn unless they were shown to be anovulatory in that cycle.
- Subjects who failed to conceive after 6 cycles with frozen semen were given fresh semen for 1 to 3 cycles. This treatment strategy gives a strong bias in favor of frozen! The most fertile women conceive early leaving only the relatively less fertile behind after 6 cycles to be treated with fresh semen. Despite this bias, fresh semen has slightly higher cycle fecundity.

15. Hammond MG, Jordon S, Sloan CS. Factors affecting pregnancy rates in a donor insemination program using frozen semen. *Am J Obstet Gynecol* 1986;155:480-5.

- I did not include this in the meta-analysis because it was not possible to obtain the needed data. Data analysis in this paper is especially poor and the paper is cited here only because it is listed in the bibliography of many papers on this subject.
- Fresh semen was used only after 3 to 5 failed cycles of frozen. Fresh semen was then used when available. This treatment strategy gives a strong bias in favor of frozen! The most fertile women conceive early leaving only the relatively less fertile behind after 6 cycles to be treated with fresh semen.
- The comparison in Table IV is between women who had only frozen (cycle fecundity: $56/591 = 9.5\%$) and those who had both frozen and fresh (cycle fecundity: $47/383 = 12.3\%$).