[Two and a Half Degrees of Separation: Clinical Trial Finds Moderate Cooling Improves Transplant Results](http://blog.fisherbioservices.com/two-and-a-half-degrees-of-separation-clinical-trial-finds-moderate-cooling-improves-transplant-results)

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This is not about a chain of six acquaintances that (in theory) connect all the inhabitants of the world, but rather how a very small reduction in temperature can make a tremendous difference in the outcome of an organ transplant. A recently published clinical trial1 found that establishing mild hypothermia in an organ donor resulted in a significant benefit to recipients of transplanted kidneys! So here is a question to consider: if 2.5°C has a significant effect on outcomes in living patients, what effect may it have on biospecimen-based research?

The clinical trial mentioned above, entitled Therapeutic Hypothermia in Deceased Organ Donors and Kidney-Graft Function, was published July 30 in the New England Journal of Medicine, and showed that mild hypothermia had a significant protective effect on transplanted kidneys.

Transplant organs, or sections/tissues from transplant organs are on occasion made available to or even sought by researchers and biobanks. The protocol for organ recovery for transplant purposes, like the protocol for the [collection of biospecimens](http://blog.fisherbioservices.com/top-considerations-when-establishing-a-biospecimen-collection-part-i), has a significant effect on the quality of the downstream results. In the case of a transplant patient, the difference has a great influence both on the quality and the duration of life.

We know [pre-analytical variability](http://blog.fisherbioservices.com/does-your-biosample-pre-analytical-process-measure-up) can effect on assay results, and ultimately the value of research. This clinical trial may be food for thought for those conducting research far upstream from the actual patient, as well as those who are practicing medicine.

The trial specifically focused on whether or not mild hypothermia improved the function of transplanted kidneys (measured in the time needed for the recipient to achieve independence from dialysis). The current protocols for the transplant of a kidney call for normothermia, typically involving a means of actively warming the donor to maintain a temperature between 36.5°C and 37.5°C until organ recovery could be performed.

The trial accepted only donors following declaration of death according to neurologic criteria (as well as other criteria); potential donors with a determination of circulatory death were excluded. The physiologic changes that occur with brain death include hemodynamic instability, endocrine abnormalities, pulmonary dysfunction, skewing of electrolyte balances and others; many are the result of the core temperature falling towards the ambient temperature. Given that these physiological deficiencies must be medically corrected before organ donation, maintaining a temperature of about 37°C in the donor to preserve organ function seems appropriate. However, mild hypothermia is also protective against renal injury in cases of brain trauma and other critical events.

In this context, i.e., a clinical trial of transplanted kidney function, mild hypothermia ( also termed “targeted temperature management”) meant that the donor was allowed to cool only about two degrees, to between 34°C to 35°C. However, the effect of this very mild hypothermia on kidney function following transplant was significant; the benefit was so pronounced that the trial was halted when only half the number of patient were enrolled. It was also noted that the benefit was greatest among the patients who received kidneys from extended-criteria donors—donors who were older and had more co-existing conditions, such as hypertension.

If a difference of two degrees can have such a significant impact on patients receiving transplanted tissue, how significant is it for tissues that are collected post-mortem and banked for future research? Depending on the nature of the research, it may make little difference. However, noting the conditions of the tissue collection, and appending this data to the sample is critical.

The Biospecimen Reporting for Improved Study Quality ([BRISQ](http://blog.fisherbioservices.com/brisq-or-risk-publication-of-your-research))2 recommendations published by the International Society of Biological and Environmental Repositories ([ISBER](http://blog.fisherbioservices.com/banking-on-personalized-medicine-isber-2015-annual-meeting)) include a Tier 1 Data Element for the vital state of the patient (alive / deceased) when the specimen was taken. Where samples from organ donors are accepted, addition of a Tier 2 or Tier 3 Data Element, to capture the temperature of the donor (or organ/tissue) at the time of donation or collection may also be critical.

Two more significant considerations are worth mentioning: the first is that the research represents a low-cost and simple improvement in medical practice that can have a dramatic effect on patients’ lives, something we don’t hear about very often. The second is that the researchers who conducted the clinical trial, and the New England Journal of Medicine, generously made the full article, as well as the study protocol and a supplementary appendix with additional information, fully available online.