**Tentative Course Schedule**. Updated schedules to be posted on D2L. ICH=International Conference on Harmonisation ICH\_E9 (numbers refer to pages to read); Ch refers to chapter of the Friedman et al textbook; GCP=Good Clinical Practice (ICH\_E6)

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| **Date** | **Topic** | **Guest lecturer/ topic** | **Reading** |
| Jan 20 | **Introduction**  **Why clinical trials?**  Phases I-IV | Melanie Bell/ Intro to ethics | Ch 1-2  ICH p1-4  Emanuel EJ, et al. What makes clinical research ethical? JAMA 2000;283:2701-11.  Hulley et al, Anatomy and Physiology of Research.  Mourvillier B, Tubach F, van de Beek D, et al. Induced Hypothermia in Severe Bacterial Meningitis: A Randomized Clinical Trial. JAMA. 2013;310(20):2174-2183. |
| Jan 27 | **What is the research question?**  Study population  Treatment groups  Outcomes  Composite endpoints  Surrogate endpoints  Blinding  The Protocol | Melanie Bell/  Fear of cancer recurrence RCT | Ch 3,7  ICH p 4-9  Cordoba G et al. Definition, reporting, and interpretation of composite outcomes in clinical trials: systematic review. BMJ 2010;341:c3920.  Fleming, T. R., & DeMets, D. L. (1996). Surrogate end points in clinical trials: are we being misled? *Annals of Internal Medicine, 125*(7), 605-613.  Prentice RL. Surrogate endpoints in clinical trials: definitions and operational criteria. *Stat Med* 1989; 8:431-440. |
| Feb 3 | **Randomization**  Simple  Blocked  Stratified  Minimization | Robin Harris | Ch6  ICH p9-11  Scott, NW, et al (2002). The method of minimization for allocation to clinical trials. a review. *Controlled Clinical Trials, 23*(6), 662-674. |
| Feb 10  HW1 due | **Experimental design**  Parallel group  Crossover  Factorial  Non-inferiority  Cluster | Cyndi Thompson/  Methodological issues diet & exercise | Ch5  ICH p11-18  TGN1412 paper |
| Feb 17 | **Analysis of phase III trials** |  | Ch 9 & 17  ICH p24-29 |
| Feb 24 | **Missing data**  Prevention  Analytical approaches  Reporting |  | ICH p24-25  Bell, M. L., & Fairclough, D. L. (2013). Practical and statistical issues in missing data for longitudinal patient reported outcomes. *Statistical Methods in Medical Research*. |
| Mar 3  HW2 due | **Analysis of phase III trials**  Subgroup analysis |  | ICH p26-27  Assmann, S. F., Pocock, S. J., Enos, L. E., & Kasten, L. E. (2000). Subgroup analysis and other (mis) uses of baseline data in clinical trials. The Lancet, 355(9209), 1064-1069.  Sun, X., Briel, M., Walter, S. D., & Guyatt, G. H. (2010). Is a subgroup effect believable? Updating criteria to evaluate the credibility of subgroup analyses. BMJ: British Medical Journal, 850-854. |
| Mar 10 | **Analysis of phase III trials**  Survival | Joe Gerald/  Comparative Effectiveness Research | Ch15  Boston University,   Online module on principles of survival analysis.  <http://sph.bu.edu/otlt/MPH-Modules/BS/BS704_Survival/>.  SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network. Target ranges of oxygen saturation in extremely preterm infants. *N Engl J Med* 2010;362:1959-1969  Drazen JM. Et al, Informed Consent and SUPPORT *N Engl J Med* 2013; 368:1929-1931 |
| Mar 17 |  | SPRING BREAK |  |
| Mar 24 | **More analysis** |  | Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG, for the CONSORT Group. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trial. [BMJ 2010;340:c869](http://www.bmj.com/cgi/content/full/340/mar23_1/c869). |
| Mar 31 | **Cluster RCT**  Motivation/rationale  Design  Analysis | Lynn Gerald/ CRCT, educational interventions  3-4 | Wears, R. L. (2002). Advanced Statistics: Statistical Methods for Analyzing Cluster and Cluster-randomized Data. *Academic Emergency Medicine, 9*(4), 330-341  Campbell, M. K., Elbourne, D. R., & Altman, D. G. (2004). CONSORT statement: Extension to cluster randomised trials. *British Medical Journal, 328*(7441), 702-708.  Mäusezahl D, et al, Solar Drinking Water Disinfection (SODIS) to Reduce Childhood Diarrhoea in Rural Bolivia: A Cluster-Randomized, Controlled Trial PLoS Med. 2009, 6 ( 8) |
| Apr 7 HW3 due | **Statistical analysis plan**  Essential elements  Timing  Relation to protocol  ITT and analysis sets |  | ICH p21-24  GCP 30-33  Adams-Huet B, et al.  Bridging clinical investigators and statisticians: writing the statistical methodology for a research proposal.  J Investig Med 2009; 57:818-24.  Hollis, S., & Campbell, F. (1999). What is meant by intention to treat analysis? Survey of published randomised controlled trials. *British Medical Journal, 319*(7211), 670-674. |
| Apr 14 | **Sample size**  Continuous outcomes  Binary outcomes  Survival outcomes | Denise Roe/DSMB | Ch8  ICH p18-21  Halpern et al. (2002). The continuing unethical conduct of underpowered clinical trials. *Journal of the American Medical Association, 288*(3), 358-362.  Livingston G, et al. Clinical effectiveness of a manual based coping strategy programme (START, STrAtegies for RelaTives) in promoting the mental health of family carers of people with dementia: pragmatic randomised controlled trial. *BMJ* 2013;347:f6276. |
| Apr 21 | **Monitoring**  Group sequential methods/  Interim analysis  Adverse events | Chris Bime/ multicenter trials, practical issues | Ch12, 16  ICH p18-21  Fleming, T. R., Ellenberg, S., & DeMets, D. L. (2002). Monitoring clinical trials: issues and controversies regarding confidentiality. *Statistics in Medicine, 21*(19), 2843-285  Hammer SM et al. (2013) Efficacy trial of a DNA/rAd5 HIV-1 preventive vaccine. N Engl J Med |
| Apr 28 | **Phase I & II**  **Pilot studies**  **Non-inferiority** |  | ICH p14-16  Pocock, S. J. (2003). The pros and cons of noninferiority trials. *Fundamental and Clinical Pharmacology, 17*(4), 483-490.  Thabane, L., et al (2010). A tutorial on pilot studies: the what, why and how. *BMC Medical Research Methodology, 10*, 1.  Merchant et al. (2012) Phase I Trial and Pharmacokinetic Study of Lexatumumab in Pediatric Patients With Solid Tumor |
| May 5 HW4 due | **Presentations** |  | ICH p29-32  Gelfond, et al (2011). Principles for the ethical analysis of clinical and translational research. *Statistics in Medicine, 30*(23), 2785-2792 |

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