Abstract: Although randomized control trials represent the gold standard of evidence in clinical research, there exist logistical or ethical scenarios that make it infeasible to randomize subjects. Such cases have led researchers to adopt alternative, observational, study designs such as matched case-control (MCC). MCC studies aim to minimize confounding by “matching” subjects who exhibit an outcome of interest (cases) with records of similar individuals who do not (controls). While this pairing offers a means to study associations between exposures and outcomes, the quality of study results relies heavily on the identification of appropriate control subjects. Unfortunately, criteria to match subjects remains subjective, often requiring researchers be aware of confounding factors a-priori. This discretionary selection can vary between study teams and raises the possibility more appropriate control subjects may exist if additional factors were considered. This talk will highlight research developing a novel computational framework to empirically identify optimal control subject(s) in matched case control studies using a complete set of patient data. By removing human bias of selecting matching factors, we will discuss improvements in matched pair alignment and discuss ongoing work to extend the framework to capture temporal patterns of patient data.