Supporting information 2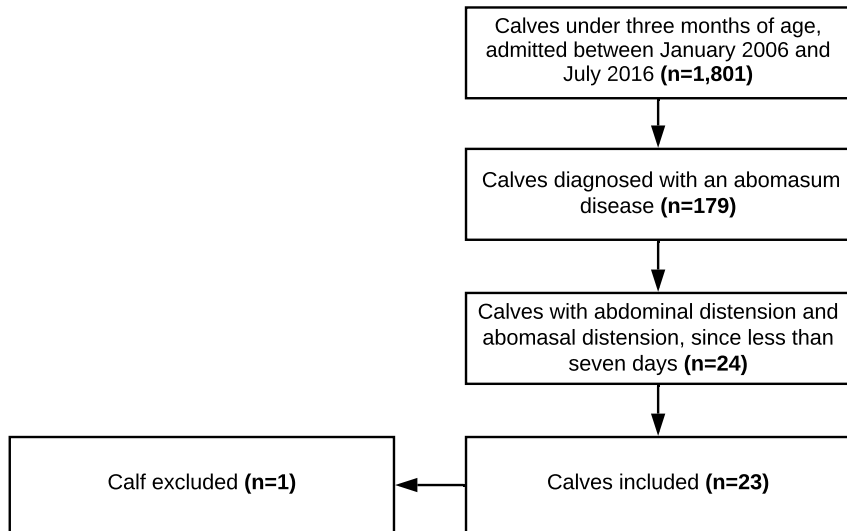: Flow diagram