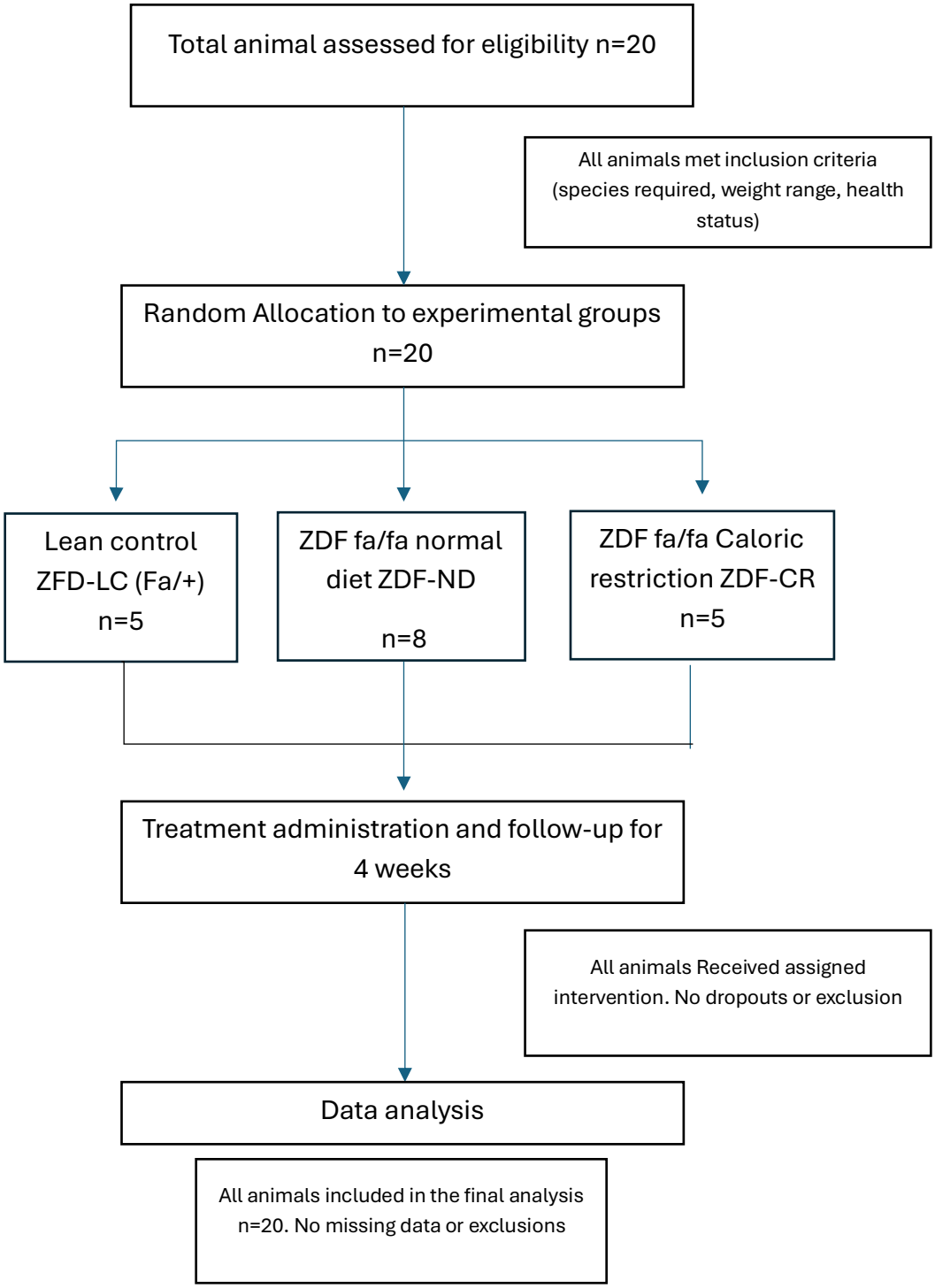S1: Experimental design and Animal Allocation Flow Chart