The author discusses the application of a massive variable flavor number scheme for the Drell-Yan process and uses standard factorization of QCD hard scattering cross sections with massive quarks in the limit of small quark masses, essentially exploiting the role of the heavy quark mass as a collinear regulator.

The explicit application to the Drell-Yan process at order α_s^2 and partial results at α_s^3 are novel. This merits publication in SciPost.

The current version of the manuscript has a number of weaknesses, which the author could consider to resolve.

1. The discussion in sec.2 is rather generic and eq.(3) could be explained in more detail. Also the quantity $\Delta_{n_f}^{(i)}$ should be given explicitly.

2. The discussion of the heavy quark mass slicing in sec.3 needs better explanation of the technical details, of eq.(4) and the comments below it.

3. The comment on the intrinsic charm distribution in the proton is somewhat out of context and leaves important questions open, for example the form of the evolution equations for massive quarks. When the heavy-quark mass acts as a collinear regulator, but singularities do remain for initial massive quarks, the concept of collinear factorization is at stake.

4. The discussion of the computational set-up is rather generic, as it relies on an extensive list of external results, which are only mentioned in a summary manner. It is not clear, which results of those references have been used.

   For example, the OMEs of ref.[24] use a particular renormalization scheme for α_s and the quark mass.

   Based on the present description, it does not seem possible to repeat the computation and to verify the correctness of individual components.

   Also the matching of the heavy quark parton distribution is unclear. As mentioned, the definition of the parton distributions with intrinsic charm as done in the NNPDF3.1 set used in the computation raises questions. It is unclear, if the charm quark parton distribution at the initial scale matches perturbative decoupling and fulfills energy momentum conservation.

5. Sec.8 discusses recommendations to the LHCb experiment, which is again a bit out of scope given the main thrust of the study.