Fair Evaluation in Concept Normalization: a Large-scale Comparative Analysis for BERT-based Models

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Abstract

Linking of biomedical entity mentions to various terminologies of chemicals, diseases, genes, adverse drug reactions is a challenging task, often requiring non-syntactic interpretation. A large number of biomedical corpora and state-of-the-art models have been introduced in the past five years. However, there are no general guidelines regarding the evaluation of models on these corpora in single- and cross-terminology settings. In this work, we perform a comparative evaluation of various benchmarks and study the efficiency of state-of-the-art neural architectures based on Bidirectional Encoder Representations from Transformers (BERT) for linking of three entity types across three domains: research abstracts, drug labels, and user-generated texts on drug therapy in English. We have made the source code and results available at https://github.com/insilicomedicine/Fair-Evaluation-BERT.

1 Introduction

Aggregating knowledge about entities across different domains and corpora is critical for many information extraction (IE) applications. In biomedical research and healthcare, the entity linking problem is known as medical concept normalization (MCN). Medical concepts may have different types (e.g., drugs, diseases, or genes/proteins) and may be retrieved from different single-typed ontologies. Effective mapping of the same concepts across different ontologies (the MCN task) is the holy grail of modern medical NLP.

Most MCN methods meanwhile are evaluated on test sets of widely differing sizes and domains and a narrow subsample of concepts from specific terminology. Moreover, the reported results of neural networks vary substantially on different corpora, with, for example, accuracy ranging at least from 91% to 96% on research abstracts (Sung et al., 2020) and accuracy from 77% to 89% on social media texts (Miftahutdinov and Tutubalina, 2019).

Owing to their superior semantic learning capabilities, BERT (Devlin et al., 2019) and other neural architectures have been widely used in recent state-of-the-art (SOTA) models for the MCN task on research abstracts and social media texts (Leaman and Lu, 2016; Zhao et al., 2019; Li et al., 2017; Phan et al., 2019; Wright et al., 2019; Sung et al., 2020; Miftahutdinov and Tutubalina, 2019; Ji et al., 2020). These studies mostly share the same limitations regarding their evaluation strategy: models are usually trained and evaluated on entities of the same type from a single domain. Often, concept unique identifiers (CUIs) used in training are included in the test set. A recurring problem, which arises with supervised models, is how to reuse trained models for a different purpose; this requires coding to a specific terminology. In this work, we take the task a step further from existing research by exploring current benchmarks and cross-terminology transfer between entity mentions in research abstracts, drug labels, and user-generated texts.

We perform an extensive evaluation of five biomedical corpora manually annotated with concepts regarding diseases, chemicals, human genes, and adverse drug reactions (ADRs). We utilize two models:
Table 1: Statistics of the datasets used in our experiments.

(i) a baseline that ranks concepts for a given mention by comparing biomedical BERT vectors (Lee et al., 2019) with the Euclidean distance; (ii) a supervised SOTA model BioSyn (Sung et al., 2020). The work reported here aims to advance SOTA models in biomedical concept normalization of entity mentions with a variety of entity types and differences in surface characteristics of mentions. In this work, we seek to answer the following research questions: **RQ1:** Do test sets of current benchmarks lead to an overestimation of performance? **RQ2:** How do surface characteristics of entity mentions affect the performance of the BERT-based baseline? **RQ3:** Does a model trained on one corpus work for the linking of entity mentions of another type or domain in the zero-shot setting?

## 2 Datasets and Resources

We use the following publicly available benchmarks with official train/dev/test splits. Descriptive statistics of these datasets are shown in Table 1.

**NCBI Disease Corpus** The NCBI Disease Corpus (Do˘gan et al., 2014) contains 793 PubMed abstracts with disease mentions and their concepts corresponding to the MEDIC dictionary (Davis et al., 2012). The NCBI corpus is the smallest (by the number of mentions), but the mentions have the longest average length and most of them are related to cancer and tumors. This MEDIC dictionary integrates concepts and synonyms from the Online Mendelian Inheritance in Man (OMIM) (Amberger et al., 2011) and the “Diseases” category of the National Library of Medicine’s Medical Subject Headers (MeSH) (Coletti and Bleich, 2001). The “Diseases” category is very broad in MeSH; it includes conditions generally recognized as disease, abnormalities, injuries, poisoning, addiction, and pathological signs and symptoms. We use the MEDIC lexicon (v. July 6, 2012) that contains 11,915 CUIs and 71,923 synonyms.

**BioCreative V CDR** BioCreative V CDR (BC5CDR) (Li et al., 2016) introduces a task for the extraction of chemical-disease relations (CDR) from 1500 PubMed abstracts that contains annotations of both chemical/diseases. When dealing with chemicals, it is likely to see them expressed in the text exactly as they are seen in other abstracts: only 7.9% of mentions in the test set were unique or were not included in the train set. Disease and chemical mentions are linked to the MEDIC (Davis et al., 2012) and the Comparative Toxicogenomics Database (CTD) (Davis et al., 2019) dictionaries, respectively. We note
that CTD’s chemical vocabulary is a modified subset of descriptors from the “Chemicals and Drugs” category and Supplementary Concept Records from MeSH. This category is very broad in MeSH; it includes therapeutic drugs, pure chemicals, and a variety of biological substances. The terms “drugs” and “chemicals” are often used interchangeably. We utilize the CTD chemical dictionary (v. November 4, 2019) that consists of 171,203 CUIs and 407,247 synonyms.

**BioCreative II GN** BioCreative II GN (BC2GN) (Morgan et al., 2008) contains PubMed abstracts with human gene and gene product mentions for gene normalization (GN) to Entrez Gene identifiers (Maglott et al., 2005). Gene mentions have the shortest average length and 62.46% contain numerals. To create the lexicon, we took the gene symbol, alias and description information for each gene identifier matched the following query on NCBI1: “‘Homo sapiens’[porgn] AND alive[prop]”. It contains 61,646 CUIs and 277,944 synonyms.

**TAC 2017 ADR** TAC 2017 ADR (Roberts et al., 2017) proposes a challenge for the extraction of ADRs found in product labels (prescribing information or package inserts). ADRs are manually mapped into the MedDRA dictionary (Brown et al., 1999). In this study, we use MedDRA v19.0 which contains 24,033 CUIs and 77666 synonyms.

**SMM4H 2017 ADR** The Social Media Mining for Health (SMM4H) challenge (Sarker et al., 2018) presents a dataset with annotated ADR mentions linked to MedDRA. Tweets were collected using 250 generic and trade names for therapeutic drugs. Manually extracted ADR expressions were mapped to Preferred Terms (PTs) of the MedDRA dictionary. We use MedDRA v19.0 for this dataset. Out of the above-mentioned corpora, this corpus has the largest intersection of concepts between sets: 85% of concepts from the test set were present in the train set.

### Preprocessing

Similar to previous works (Leaman and Lu, 2016; Wright et al., 2019; Phan et al., 2019; Sung et al., 2020), we use several preprocessing steps. In particular, we adopt preprocessing scripts for datasets and dictionaries from the work (Sung et al., 2020). We use Ab3P (Sohn et al., 2008) to detect local abbreviations and replace each instance with the corresponding long form. We use heuristic rules (D’Souza and Ng, 2015) to split composite mentions into separate mentions (e.g., non-familial breast and ovarian cancers into non-familial breast cancer and ovarian cancers). Entity mentions from a training set are included in a corpus-specific dictionary. Finally, we process all characters to lowercase forms and remove punctuation for both mentions and synonyms.

#### 2.1 Isolating train and test entity mentions

Given predefined splits of NCBI Disease, BC5CDR, and TAC 2017 ADR datasets, recent neural models achieve almost excellent accuracy averaging between 91% and 96% (Phan et al., 2019; Sung et al., 2020). Hence, one could view the MCN task on scientific texts as a largely solved task. After our analysis of datasets, we found out that approximately 80% entity mentions in the test set are textual duplicates of other entities in the test set or entities presented in train+dev sets. In order to obtain more realistic results, we present refined test sets without duplicates or exact overlaps. We note that some concepts appearing in the refined test set also appear in the respective training set (see \( |T_1 \cap T_3| \) in Table 1).

In future work, we suggest that refined test sets can be split into two subsets, stratified and zero-shot. Here Stratified (Tutubalina et al., 2018) is intended to show how well models recognize known concepts with different surface forms of entity mentions. In contrast, the zero-shot setting shows how well models map mentions to novel concepts. Here we present a cross-terminology evaluation that is a more complicated version of zero-shot evaluation due to a shift in entity type and surface form mentions.

### 3 Models for Concept Normalization

We utilize two BERT-based models: (i) a baseline method based on the ranking of BioBERT representations, (ii) a SOTA model named BioSyn (Sung et al., 2020). We use BioBERT\textsubscript{base} v1.1 for both models that was pre-trained on PubMed abstracts (4.5B words in total) for 1M steps.

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1https://www.ncbi.nlm.nih.gov/
BioBERT ranking  This is a baseline model that used the BioBERT model for encoding mention and concept representations. Each entity mention or concept name is passed first through BioBERT and then through a mean pooling layer to yield a fixed-sized vector. The inference task is then reduced to finding the closest concept name representation to entity mention representation in a common embedding space. We use the Euclidean distance as the distance metric. The nearest $k$ concept names are chosen as top-$k$ concepts for entities.

BioSyn  BioSyn (Sung et al., 2020) is a recent SOTA model that utilizes the synonym marginalization technique and iterative candidate retrieval. The model uses two similarity functions based on sparse and dense representations, respectively. The sparse representation encodes the morphological information of given strings via TF-IDF, the dense representation encodes the semantic information gathered from BioBERT. BioSyn achieves SOTA results on NCBI, BC5CDR, TAC sets over previous works (Leaman and Lu, 2016; Wright et al., 2019; Phan et al., 2019). We have used the publicly available code provided by the authors at https://github.com/dmis-lab/BioSyn and reproduced the results successfully. We follow the default parameters of BioSyn as shown in (Sung et al., 2020): the number of top candidates $k = 20$, the mini-batch size is 16, the learning rate is $1e^{-5}$, the dense ratio for candidate retrieval is 0.5. We have trained BioSyn for 20 epochs for all datasets.

4 Single- and Cross-terminology Evaluation

We train BioSyn on the train/dev set of each corpus with a source dictionary, evaluating it on the respective test set (in-domain performance). For cross-domain evaluation, we assess models trained on source data on the test sets of all other corpora (i.e., the target). Specifically, both BioSyn and BioBERT ranking models retrieve the nearest concept name in a target dictionary for a given mention representation at inference time. We note that cross-terminology evaluation provides a challenging setup for developing supervised models, especially for linking to concepts not encountered during training (zero-shot concepts).

We evaluate this task in information retrieval (IR) scenario, where the goal is to find within a dictionary of concept names and their identifiers the top-$k$ concepts for every entity mention in the texts. Let $\text{acc}@k$ be 1 if the correct CUI is retrieved at rank $k$, otherwise 0. For composite entities, we define $\text{acc}@k$ as 1 if every prediction for a single mention is correct. In particular, we use the top-1 accuracy as an evaluation metric, following previous works (Suominen et al., 2013; Pradhan et al., 2014; Wright et al., 2019; Phan et al., 2019; Sung et al., 2020).

Table 2 shows results on six sets where models are usually trained and evaluated on entities of the same type from a single domain. Table 3 compares the performance of BioSyn in single- and cross-terminology normalization tasks. Models were trained on the training set from a source dataset and evaluated on the target test set with different terminology.

To answer RQ1, we compare the results of models on official and refined test sets in Table 2. The significant decrease of averaged $\text{acc}@1$ from 91.8% to 76.7% for BioSyn and averaged $\text{acc}@1$ from 77.7% to 54.9% for BioBERT ranking highlights the great need for external evaluation datasets, where the same entity mentions will not be used for both training and testing. These observations also mean that there is room for improvement in the transferability of developed methods, that is, the ability to maintain performance for entirely unseen domains or entities.

According to Table 2, the following conclusions can be drawn to answer RQ2. First, the simple ranking of BioBERT representations achieves strong results on CDR Disease and Chemical sets. On two refined sets with larger mentions (NCBI, TAC) and the BC2GN corpus with mentions containing numerals, the difference between BioBERT ranking and BioSyn is significant (average decrease of 23.6%). Our qualitative analysis uncovered that BERT representations of mentions differing by one numeral (e.g., genes TP53 and TP63) are close in the latent space. As expected, results on SMM4H are significantly lower than on abstracts due to the gap between the language of lay public and medical professionals.

To answer RQ3, we compare performance differences in Tables 2 and 3. The models trained on NCBI, CDR Disease, BC2GN, and TAC data perform on par with the model trained on the CDR Chemical train set (approx. 74% $\text{acc}@1$), while the model trained on CDR Chemical showed a 6% drop on these subsets.
### Table 2: Single-terminology normalization results in terms of acc@1 on the official and refined test sets.

| Train set | NCBI Disease | BC5CDR Dis | BC5CDR Chem | BC2GN Gene | TAC ADR | SMM4H ADR |
|-----------|--------------|------------|-------------|------------|---------|-----------|
| Test set  |              |            |             |            |         |           |
| NCBI Disease | 72.5 | 67.6 (-4.9) | 64.7 (-7.8) | 67.2 (-5.4) | 67.6 (-4.9) | 48.5 (-24.0) |
| BC5CDR Dis | 74.7 (+0.6) | 74.1 | 73.4 (-0.8) | 73.1 (-1.1) | 74.9 (+0.8) | 58.3 (-15.8) |
| BC5CDR Chem | 82.4 (-1.4) | 84.2 (+0.5) | 83.8 | 82.6 (-1.2) | 82.4 (-1.4) | 73.9 (-9.9) |
| BC2GN Gene | 83.1 (-2.6) | 81.7 (-4.1) | 83.7 (-2.1) | 85.8 | 82.6 (-3.1) | 73.2 (-12.6) |
| TAC ADR | 74.3 (-8.9) | 77.5 (-5.7) | 70.1 (-13.0) | 69.9 (-13.3) | 83.2 | 51.5 (-31.7) |
| SMM4H ADR | 27.3 (-33.2) | 35.6 (-24.9) | 24.8 (-35.7) | 21.9 (-38.6) | 30.1 (-30.4) | 60.5 |

### Table 3: Comparison of BioSyn for single- and cross-terminology MCN on refined test sets by accuracy@1. In-domain results are on the diagonals (with a dark gray background). Other cells contain results of a given model and differences in results between that model and the in-domain model in parentheses (by row). Light gray cells show cross-terminology experiments.

| Train set | NCBI Dis | BC5CDR Dis | BC5CDR Chem | BC2GN Gene | TAC ADR | SMM4H ADR |
|-----------|----------|------------|-------------|------------|---------|-----------|
| Test set  |          |            |             |            |         |           |
| NCBI Disease | 72.5 | 67.6 (-4.9) | 64.7 (-7.8) | 67.2 (-5.4) | 67.6 (-4.9) | 48.5 (-24.0) |
| BC5CDR Dis | 74.7 (+0.6) | 74.1 | 73.4 (-0.8) | 73.1 (-1.1) | 74.9 (+0.8) | 58.3 (-15.8) |
| BC5CDR Chem | 82.4 (-1.4) | 84.2 (+0.5) | 83.8 | 82.6 (-1.2) | 82.4 (-1.4) | 73.9 (-9.9) |
| BC2GN Gene | 83.1 (-2.6) | 81.7 (-4.1) | 83.7 (-2.1) | 85.8 | 82.6 (-3.1) | 73.2 (-12.6) |
| TAC ADR | 74.3 (-8.9) | 77.5 (-5.7) | 70.1 (-13.0) | 69.9 (-13.3) | 83.2 | 51.5 (-31.7) |
| SMM4H ADR | 27.3 (-33.2) | 35.6 (-24.9) | 24.8 (-35.7) | 21.9 (-38.6) | 30.1 (-30.4) | 60.5 |

**BioSyn trained on SMM4H achieves lower results on abstracts and drug labels than simple BioBERT ranking, while all supervised models performed better on SMM4H data than the BioBERT ranking.**

### 5 Conclusion

We have presented the first comparative evaluation of medical concept normalization (MCN) datasets, studying the NCBI Disease, BC5CDR Disease & Chemical, BC2GN Gene, TAC 2017 ADR, and SMM4H 2017 ADR corpora. We perform an extensive evaluation of two BERT-based models on six datasets in two setups: with official train/test splits and with the proposed test sets that represent refined samples of entity mentions. Our evaluation shows great divergence in performance between these two test sets, finding an average accuracy difference of 15% for the state-of-the-art model BioSyn. We also performed a quantitative evaluation of BioSyn in the cross-terminology MCN task where models were trained and evaluated on entity mentions of various types with concepts from different terminologies. Knowledge transfer can be effective between diseases, chemicals, and genes with an average drop of 2.53% accuracy in the performance on NCBI, BC5CDR, and BC2GN sets. For TAC and SMM4H sets with ADRs from drug labels and social media, BioSyn models trained on four other corpora show a substantial decrease in performance (-10.2% and -33.1% accuracy, respectively) compared to in-domain trained models. To our surprise, these models still outperformed the straightforward ranking baseline on BioBERT representations. We believe that refined datasets with cross-terminology evaluation can serve as a step toward reliable and large-scale evaluation of biomedical IE models.

We foresee three directions for future work. First, a promising research direction is the multilingual evaluation of MCN models. Second, in some cases current models choose a broader concept that is in a parent-child relationship with the correct concept; here future research may focus on the encoding of the concept hierarchy. Third, the use of local and global contexts of entity mentions remains to be explored.

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