CCS Explorer: Relevance Prediction, Extractive Summarization, and Named Entity Recognition from Clinical Cohort Studies

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Abstract—Clinical Cohort Studies (CCS), such as randomized clinical trials, are a great source of documented clinical research. Ideally, a clinical expert inspects these articles for exploratory analysis ranging from drug discovery for evaluating the efficacy of existing drugs in tackling emerging diseases to the first test of newly developed drugs. However, more than 100 articles are published daily on a single prevalent disease like COVID-19 in PubMed. As a result, it can take days for a physician to find articles and extract relevant information. Can we develop a system to sift through these articles faster and document the crucial takeaways from each of these articles? In this work, we propose CCS Explorer, an end-to-end system for relevance prediction of sentences, extractive summarization, and patient, outcome, and intervention entity detection from CCS. CCS Explorer is packaged in a web-based graphical user interface where the user can provide any disease name. CCS Explorer then extracts and aggregates all relevant information from articles on PubMed based on the results of an automatically generated query produced on the back-end. For each task, CCS Explorer fine-tunes pre-trained language representation models based on transformers with additional layers. The models are evaluated using two publicly available datasets. CCS Explorer obtains a recall of 80.2%, AUC-ROC of 0.843, and an accuracy of 88.3% on sentence relevance prediction using BioBERT and achieves an average Micro F1-Score of 77.8% on Patient, Intervention, Outcome detection (PIO) using PubMedBERT. Thus, CCS Explorer can reliably extract relevant information to summarize articles, saving time by \( \sim 660 \times \).

Index Terms—named entity recognition, pico, relevance, summarization, bert, language model, evidence based medicine, transformer, randomized clinical trial, information retrieval

I. INTRODUCTION

One of the world’s largest biomedical publication databases, PubMed, has over 34 million publications. Approximately 2.5 million users perform about 3 million searches and 9 million page views on PubMed every day [1]. Over the past couple of years, 137 articles have been posted per day on PubMed on COVID-19 alone [2]. In particular, clinical Cohort Studies (CCS), which contain information on the specific results of a patient or patient population for a given therapeutic and/or condition, are considered essential for clinical research. Clinical cohort studies include randomized clinical trials, prospective cohort studies, retrospective cohort studies, case-control studies, patient case studies, and more. Clinical cohort studies typically describe a patient or patient population, the intervention(s) assessed, and the measured outcome(s).

The two major applications that require the exploration of clinical cohort studies are question-answering and meta-
analysis (Fig. 1a). Investigation of clinical cohort studies is necessary to answer questions and identify qualitative relationships. Examples of question answering include: What drugs may be repurposed or used in combination to improve disease outcomes [3]? What comorbidities are most impactful to cardiac disease outcome [4]–[7]? What patient features result in health outcome disparities [8], [9]? Exploration of clinical cohort studies is also required to perform a meta-analysis, a quantitative analysis where the results of cohort studies are aggregated to estimate an overall effect size. Estimating an overall or aggregate effect size, such as the effect of a drug on disease outcome, adjusts for disparity or bias introduced by individual study-specific features (e.g., geography, gender, age, sample size). Examples of meta-analysis include: determining overall adverse event rates with specific treatments for cancer [10], determining the overall prevalence of comorbidities in a rare neurodegenerative disease population [11], or determining the overall effect size of vaccination on SARS-CoV-2 outcome [12]–[14].

The process for manual exploration of cohort studies is iterative and time-consuming (Fig. 1b). The major steps include devising the appropriate advanced PubMed query to find articles in PubMed, reviewing the list of search title results to determine if the query resulted in the expected type or number of studies, examining the abstracts to determine if the journal article contains the desired information, and curating the article to extract the pivotal PIO elements: patient population (disease and/or control population), intervention (what therapy was utilized), and the outcome (what measurement was utilized to determine a result). Depending on the number of studies to be reviewed and included, the exploration process alone can take hours to weeks before final curation and analysis can occur [15]. Moreover, even with a quality control team, there may be some remaining inconsistency between researchers or curators [15]. Critical variations and corresponding delays may occur depending on the researcher’s knowledge of constructing an appropriate advanced PubMed query. An appropriate PubMed query must include all relevant synonyms, MESH terms, and proper formatting to return the most inclusive and relevant list of articles. Additionally, differences in review styles for examining lengthy abstracts or even full-text articles may result in unintended differences in article inclusion or stylistic differences in PIO extraction.

Although there are specially trained groups dedicated to manually synthesizing findings from CCS, the rapid publication of new articles makes it impossible to maintain pace [16]. However, Natural Language Processing (NLP) breakthroughs have enabled the automation of many time-consuming tasks related to text exploration in non-biomedical domains such as sentiment analysis of customer reviews [17], language translation [18], [19], ranking search results [20]–[22], abstractive summarization [23]–[25], and extractive summarization [26], [27].

Here we present CCS Explorer to automate the clinical cohort study exploration (Fig. 1c). CCS Explorer is an open-source web application that dramatically expedites identifying, reviewing, and extracting data from clinical cohort studies. CCS only requires that the user input a disease name. Using a pre-built list of intervention names (which can also be customized if desired), CCS Explorer formulates an advanced query to PubMed. CCS Explorer automatically obtains all relevant articles via their unique PubMed identification (PMID) and parses through the text. CCS Explorer provides three critical outputs for researchers: 1) a list of all relevant studies along with a relevance prediction score; 2) an abbreviated relevance summary that contains only the most relevant information (or sentences) necessary for the researcher to explore the study; 3) automated extraction of PIO elements. With CCS Explorer, question answering or meta-analysis is greatly expedited, streamlined, and optimized. CCS Explorer automates all the iterative, front-end work that generally takes a specially trained team of researchers hours to weeks to achieve.

CCS Explorer is an end-to-end system for exploring clinical cohort studies with PubMed and extracting useful information necessary for tasks like question answering or meta-analysis. Fig. 1 highlights the difference between manual exploration by an expert and CCS Explorer. It can reduce the time taken to extract relevant information and summarize articles from hours to seconds. For the query demonstrated in Fig. 3, it takes 26.32s for CCS Explorer to run the query, process the resulting articles, and extract all relevant information to construct a task-specific summary along with the detection of PIO entities.

![Fig. 2: CCS Explorer Framework](image-url)
We introduce two models for this task, one for relevance prediction of text and another for detecting participant, intervention, and outcome (PIO) entities in CCS articles. We compare the proposed models’ performance by initializing the weights using 6-7 different pre-trained BERT [28], and ELECTRA [29] models.

The main contribution of this paper is to design each of the following pieces and combine them to form CCS Explorer:

- **Web Application**: front-end designed for taking inputs from the user and displaying outputs
- **Query Generator**: merges MeSH terms to form an advanced query for PubMed to obtain PMIDs
- **Article Extractor**: extracts articles from PubMed and stores the text for subsequent steps
- **Relevance Predictor**: attention-based language model that assigns a relevance score to each sentence in the article
- **Summarizer**: generates an extractive summary of the article by putting together the most relevant sentences into a coherent body of text
- **PIO Detector**: named entity recognition model finds participants, interventions, and outcomes present in the article and assigns a score for each entity

The resulting framework of CCS Explorer is shown in Fig. 2.

**II. SYSTEM DESIGN**

The goal of CCS Explorer is to provide a user-friendly system for researchers to obtain reliable results expeditiously. To this end, Streamlit [30] was used to design an intuitive front-end user interface for CCS Explorer. The graphical user interface, GUI, is shown in Fig. 3. It takes inputs from the user and displays the results in a user-friendly format for review. CCS Explorer comprises of the following:

- **Step 1**: This encompasses the creation of the query. The user has two options: (1) create a manual query by stitching together MeSH terms (2) provide a disease name so that the **Query Generator** can build an advanced query for PubMed. The query is named to enable usage in subsequent steps.
- **Step 2**: A query name has to be selected from the options provided consisting of previously formed queries. PMIDs are obtained from PubMed based on the selected query.
- **Step 3**: The articles are extracted from PubMed using the PMIDs, and **Relevance Predictor**, **Summarizer**, and **PIO Detector** are run on each article to obtain aggregated results. This step is not visible in Fig. 3 since it is complete, and the user has moved on to the next step.
- **Step 4**: Three tables show the results of **Relevance Predictor**, **Summarizer**, and **PIO Detector**.

CCS Explorer can be divided into three different pieces which run in the back-end: (1) **Query Generator** and **Article Extractor**, (2) **Relevance Predictor** and **Summarizer**, (3) **PIO Detector**. The details of **Relevance Predictor** are discussed in Section III and **PIO Detector** in Section IV. The framework of CCS Explorer is shown in Fig. 2.
Query Generator and Article Extraction. CCS Explorer provides the users with a graphical user interface to input their National Center for Biotechnology Information (NCBI) email and API key to enable repeated PubMed queries. It also allows the user to manually input a customized advanced query using MeSH terms or to provide a cancer type so that an automatically generated query can obtain a baseline result. The query generation and extraction of articles are performed using BioPython [31], [32]. Each of the resulting texts is prepared for subsequent steps using SciSpacy [33].

III. RELEVANCE PREDICTION AND EXTRACTIVE SUMMARIZATION

A. Data

The data used in building the Relevance Predictor and Summarizer of CCS Explorer originate from an open source dataset called the Evidence Inference dataset [34]–[36]. It contains valuable annotations of relevant information in CCS articles.

In this dataset, [34]–[36], groups of text are labeled as evidence and nonevidence. In designing CCS Explorer, we replaced the evidence label with relevant and non-evidence with irrelevant. The resulting relevant and irrelevant labels were used as ground truth annotations to build the Relevance Predictor of CCS Explorer. It consists of 4,005 unique articles split across two partitioned sets. The selection of articles for training and test set was defined in the Evidence Inference [34], [35] dataset as train_article_ids and validation_article_ids, respectively.

The Summarizer uses results from the Relevance Predictor to formulate summaries and a Summary Score to denote its quality.

B. Method

Relevance Prediction. Relevance Predictor was designed using BERT-based language models pre-trained on scientific articles obtained from sources such as PubMed, PubMed Central, and UMLS. It was constructed by adding a dense layer to the pre-trained model architecture and fine-tuned on the Evidence Inference dataset described in Section III-A.

The pre-trained BERT models used:

- BioBERT [37]: Initialized using standard BERT [28] model, and then pre-trained on Biomedical domain texts, which includes PubMed abstracts and PubMed Central full-text articles.
- PubMedBERT [38]: Pre-trained a BERT [28] model from scratch using 14 million abstracts from PubMed.
- SapBERT [39]: Pre-trained a BERT model on the biomedical knowledge graph of UMLS [40] using self-alignment to cluster synonyms of the same concept.
- BlueBERT [41]: Initialized using standard BERT [28] model and pre-trained on PubMed abstracts (4 Billion words) and clinical notes from MIMIC-III (500 Million words) [42].
- KRISSBERT [43]: Initialized with PubMedBERT [38] parameters, and then pre-trained using biomedical entity names from the UMLS ontology [40] to self-supervise entity linking examples from PubMed abstracts.
- SciBERT [44]: Trained a BERT [28] model on scientific papers taken from 1.14 million full papers from Semantic Scholar.

Let \(Y\) be all the outputs from the model, \(Y_r\) be all the annotations from the dataset, \(y_i\) represent the model prediction, and \(y_i\) denote the annotation of the \(i\)-th sentence. Let \(h(x_i)\) represent the output of the transformer architecture. This output, \(h(x_i)\), is used as input to a fully-connected layer followed by the sigmoid function \(\sigma\). So, the output of the model for the \(i\)-th sentence is represented by:

\[
z_i = W^T h(x_i) + b \Rightarrow y_i = \sigma(z_i) = \frac{1}{1 + e^{-z_i}} \tag{1}\]

Binary cross entropy loss is used and is denoted by:

\[
L(y_i, y'_i) = -[y_i \cdot \log(y'_i) + (1 - y_i) \cdot \log(1 - y'_i)] \tag{2}\]

Summarization. The output of the sigmoid function \(\sigma\) in Equation (1), \(y'_i\), represents the relevance score for the \(i\)-th sentence. The sentences are then sorted in descending order by these relevance scores to generate the set of sentences \(Y_{sorted}\) sorted.

The first 4 sentences corresponding to the 4 most relevant sentences are joined to form the extractive summary for each article. The summary score is the average of the relevance scores for each of these 4 sentences.

\[
\text{Summary Score} = \frac{\sum_{i=1}^{4} y_i_{sorted}}{4} \tag{3}\]

Metrics. The following metrics were used to evaluate the performance of the relevance prediction model:

\[
\begin{align*}
\text{Accuracy} &= \frac{|Y \cap Y_r|}{N} \\
\text{Recall}, R &= \frac{|Y \cap Y_r|}{|Y|} \\
\text{Precision}, P &= \frac{|Y \cap Y_r|}{|Y_r|} \\
\text{F1 score} &= \frac{2 \cdot P \cdot R}{P + R}
\end{align*} \tag{4}
\]

where the annotated relevance labels of the entire dataset are denoted by \(Y\) and the model predictions by \(Y_r\); \(|Y|\) and \(|Y_r|\) represent the number of annotated tokens and the number of model predictions. In addition to the above metrics, the area under the receiver operating characteristics curve (AUC-ROC) is used for comparison.

Implementation Details. We implemented Relevance Predictor using PyTorch [45], [46] and transformers [47]. The model was trained using a machine equipped with Intel Xeon Gold 6136 Processor, 376GB RAM, an Nvidia V100 GPU, and CUDA 11.4. During training, we used a batch size of 16, and a learning rate of 10\(^{-5}\). Each model was trained for 4 epochs.
using ADAM [48] as the optimization method. The 3,562 articles defined in train_article_ids are used as the training set, and the 443 articles specified in validation_article_ids list are used as the test set from the Evidence Inference Dataset [34], [35].

**C. Result**

A high recall is essential for relevance prediction to detect all relevant sentences. It is acceptable for an automated system to include some irrelevant sentences as long as the significant ones appear at the top of the list. Prior research in machine translation show alignment with human expectation is highest when the optimization focuses on recall [59]. User evaluation of interactive information retrieval performance [60] indicates recall is significantly more correlated with the users' expectation of success. Similarly, recall is more important than precision for downstream tasks such as summarization [61]. Most of the evaluated models for relevance prediction displayed a recall above 80%, AUC-ROC above 84%, and accuracy above 88%. The low F1-score is due to the low precision, which is less critical for tasks such as relevance prediction [59]–[61]. Due to the highest average metrics among all methods, BioBERT [37] was selected as the model used to make relevance predictions in the back-end of the web-based interface of CCS Explorer.

**Case Study.** An example of the relevant sentence prediction and subsequent summary formulation using CCS Explorer for a PubMed query targeting colorectal cancer articles is demonstrated in Fig. 4. The article obtains a Summary Score of 0.588 using Summarizer. In this article, titled Beta-blockers may reduce intrusive thoughts in newly diagnosed cancer patients by Lindgren et al. [56], the highest scoring sentence perfectly summarizes the goal of the study. The second sentence provides an example of potential problems faced by the cohort. The third sentence focuses on the study’s results, and the fourth concludes the study. The summary score is obtained by averaging the relevance score of each sentence forming the summary. The summary scores of all the articles resulting from the query are shown in Table II. It shows that the model is consistent and obtains a good summary score for all articles, with a maximum score of 0.631 and a minimum score of 0.537.

![Image of Table I: CCS Explorer: Relevance Prediction Model Performance](image)

| Model          | Accuracy | Precision | Recall | AUC-ROC | F1-Score |
|----------------|----------|-----------|--------|---------|----------|
| BioBERT [37]   | 0.883    | 0.083     | 0.802  | 0.843   | 0.150    |
| PubMedBERT [38]| 0.880    | 0.080     | 0.801  | 0.841   | 0.145    |
| SapBERT [39]   | 0.887    | 0.083     | 0.776  | 0.832   | 0.149    |
| BlueBERT [41]  | 0.875    | 0.078     | 0.817  | 0.846   | 0.143    |
| KRISSBERT [43] | 0.884    | 0.082     | 0.792  | 0.839   | 0.149    |
| SciBERT [44]   | 0.877    | 0.080     | 0.814  | 0.846   | 0.145    |

**Objective:** A cancer diagnosis provokes significant levels of emotional distress, with intrusive thoughts being the most common manifestation among breast cancer survivors. Cancer-related intrusive thoughts can take the form of emotional memories, flashbacks, nightmares, and intrusive images. Emotional arousal after a severe life stressor prolongs adrenocortical activation, which in turn may increase risk for post-traumatic symptomatology. However, antipersistent beta-blockers block adrenocortical activation and are known to reduce traumatic memories and related psychological distress. Thus, the current study examined the association between beta-blocker use and the severity of cancer-related intrusive thoughts and related symptoms following a cancer diagnosis. Cancer-related intrusive thoughts can take the form of emotional memories, flashbacks, nightmares, and intrusive images. Emotional arousal after a severe life stressor prolongs adrenocortical activation, which in turn may increase risk for post-traumatic symptomatology. However, antipersistent beta-blockers block adrenocortical activation and are known to reduce traumatic memories and related psychological distress. Thus, the current study examined the association between beta-blocker use and the severity of cancer-related intrusive thoughts and related symptoms following a cancer diagnosis. Cancer-related intrusive thoughts can take the form of emotional memories, flashbacks, nightmares, and intrusive images. Emotional arousal after a severe life stressor prolongs adrenocortical activation, which in turn may increase risk for post-traumatic symptomatology. However, antipersistent beta-blockers block adrenocortical activation and are known to reduce traumatic memories and related psychological distress. Thus, the current study examined the association between beta-blocker use and the severity of cancer-related intrusive thoughts and related symptoms following a cancer diagnosis.

**Methods:** The 174 breast and 36 female colorectal cancer patients who had recently undergone diagnostic screening or biopsy included 39 beta-blocker users and 171 non-users. Prior to any cancer treatment including surgery, participants completed questionnaires that included the Impact of Events Scale and the Center for Epidemiologic Studies Depression Scale. Analyses controlled for age, education, cancer stage, cancer type, days since diagnosis, marital status, depression, and comorbidities.

**Results:** Although the high rates of cancer-related distress in this sample were similar to those of other studies with recently diagnosed patients, beta-blocker users endorsed 32% fewer cancer-related intrusive thoughts than non-users.

**Conclusions:** Recently diagnosed cancer patients using beta-blockers reported less cancer-related psychological distress. These results suggest that beta-blocker use may benefit cancer patients' psychological adjustment following diagnosis, and provide a promising direction for future investigations on the pharmacological benefits of beta-blockers for cancer-related distress.

**IV. PATIENT, INTERVENTION, OUTCOME DETECTION**

**A. Data**

The final component of CCS Explorer is aimed at entity recognition of Patient, Intervention, and Outcome in clinical cohort studies. To train PIO Detector for this task, we used the EBM-NLP corpus [62]. The dataset includes 4,970 medical article abstracts with annotations indicating text sequences describing the Participants, Interventions, and Outcome elements of the respective CCS. 4,782 abstracts in the dataset are annotated using crowd-sourced labels. 188 abstracts contain annotations from domain experts with medical training. This test set with gold labels from domain experts is held-out during training and only used to test the performance of the final PIO Detector models.

**B. Method**

The pre-trained models are used for PIO Detector:

- BioELECTRA [63]: Pre-trained an ELECTRA model on full-text articles from PubMed and PubMed Central.
- PubMedBERT [38]: Pretrained a BERT model from scratch using 14 million abstracts from PubMed.
- SciBERT [44]: Pre-trained a BERT model using scientific papers taken from 1.14 million full papers from Semantic Scholar.
- BioBERT [37]: Initialized using standard BERT [28] model, and then pre-trained on Biomedical domain texts, which includes PubMed abstracts and PubMed Central full-text articles.
TABLE II: CCS Explorer generated extractive summaries of the following query: ("colorectal" AND (neoplasm OR cancer OR tumour)) OR "Colorectal neoplasms" [MeSH]) AND ("Adrenergic beta-antagonists" [MeSH] OR "Antihypertensive Agents" [MeSH] OR "beta-blockers") AND ("Cancer Survivors" [MeSH] OR "cancer survivorship" OR "cancer survivors" OR "cancer survival")

| PMID       | Title                                                                 | Journal                                                | Summary Score |
|------------|----------------------------------------------------------------------|--------------------------------------------------------|---------------|
| 26059955   | β-Blocker usage and colorectal cancer mortality: a nested case-control study in the UK Clinical Practice Research Datalink cohort. | Annals of oncology                                      | 0.537         |
| 35881046   | Beta-blocker use and urethelial bladder cancer survival: a Swedish register-based cohort study. | Acta oncologica (Stockholm, Sweden)                    | 0.605         |
| 20585097   | Association between perioperative beta blocker use and cancer survival following surgical resection. | European journal of surgical oncology                  | 0.631         |
| 28946174   | Impact of long-term antihypertensive and antidiabetic medications on the prognosis of post-surgical colorectal cancer: the Fujian ... | Aging                                                  | 0.600         |
| 34845550   | Providers’ mediating role for medication adherence among cancer survivors. | PLoS one                                               | 0.554         |
| 31062457   | Use of Antihypertensive Medications and Survival Rates for Breast, Colorectal, Lung, or Stomach Cancer. | American journal of epidemiology                       | 0.566         |
| 35728518   | β-blockers and breast cancer survival by molecular subtypes: a population-based cohort study and meta-analysis. | British journal of cancer                              | 0.568         |
| 23254559   | Beta-blockers may reduce intrusive thoughts in newly diagnosed cancer patients. | Psycho-oncology                                        | 0.588         |
| 30917833   | Cardiovascular medication use and risks of colon cancer recurrences and additional cancer events: a cohort study. | BMC cancer                                             | 0.551         |
| 21453301   | Does β-adrenoceptor blocker therapy improve cancer survival? Findings from a population-based retrospective cohort study. | British journal of clinical pharmacology              | 0.565         |

- BlueBERT [41]: Initialized using standard BERT [28] model and pre-trained on PubMed abstracts (4 Billion words) and clinical notes from MIMIC-III (500 Million words) [42].
- KRISSBERT [43]: Initialized with pre-trained PubMedBERT [38] parameters, and then pre-trained using biomedical entity names from the UMLS ontology [40] to self-supervise entity linking examples from PubMed abstracts.
- SapBERT [39]: Pre-trained BERT model on the biomedical knowledge graph of UMLS [40] using self-alignment to cluster synonyms of the same concept.

The labels for each token in the dataset are mapped onto the following 4 labels: Patient, Intervention, Outcome, and None. None represents tokens that are not any of these 3 target PIO entities.

Let \( y' \) be all the outputs from the model, \( y \) be all the annotations from the dataset, \( y'_i \) represent the model prediction, and \( y_i \) denote the annotation of the \( i \)-th token. Let \( h(x) \) represent the output of the transformer architecture. This output, \( h(x) \), is used as input to a fully-connected layer. So, the output of the \( i \)-th token is represented by \( y'_i = W^\top h(x_i) + b \).

To train the model, we used cross entropy loss Eq. 5:

\[
L(y_i, y'_i) = -\sum_{j=1}^{4} y_i[j] \log(y'_i[j])
\] (5)

where \( L(y_i, y'_i) \) is the estimated cross entropy loss for the \( i \)-th token between annotations \( y \in \mathbb{R}^4 \) and the predicted probabilities \( y'_i \in \mathbb{R}^4 \), \( y'_i[j] \) represents the model predictions for the \( i \)-th token and \( j \)-th entity.

**Metrics.** The following metrics were used to evaluate the performance of the NER models for PIO detection:

\[
\text{Recall, } R(k) = \frac{|\mathcal{Y}(k) \cap \mathcal{Y}^*(k)|}{|\mathcal{Y}(k)|}
\]

\[
\text{Precision, } P(k) = \frac{|\mathcal{Y}(k) \cap \mathcal{Y}^*(k)|}{|\mathcal{Y}^*(k)|}
\]

\[
F1 \text{ score } = \frac{2 \times P(k) \times R(k)}{P(k) + R(k)}
\] (6)

Given annotations \( \mathcal{Y} \), model predictions \( \mathcal{Y}' \), \( k = \{ \text{Patient}, \text{Intervention}, \text{Outcome}, \text{None} \} \) indicating the entity, \( |\mathcal{Y}(k)| \) and \( |\mathcal{Y}^*(k)| \) represent the number of annotations and model predictions with the label \( k \).

**Implementation Details.** The PIO Detector was implemented using PyTorch [45], [46] and transformers [47]. The model was trained using a machine equipped with Intel Xeon Gold 6136 Processor, 376GB RAM, an Nvidia V100 GPU, and CUDA 11.4. A batch size of 6 and a learning rate of \( 10^{-4} \) were used for training. PIO Detector was trained for 2 epochs using AdamW [64] as the optimization method.

The held-out test set was formed using the gold annotated labels in the EBM-NLP corpus [62]. The remaining articles were split randomly in a 9:1 ratio corresponding to the training and validation set and used to optimize training and set hyperparameters. The held-out test set was used to evaluate PIO Detector and compare different baselines.

**C. Result**

Table III compares the PIO Detector in CCS Explorer using different pre-trained BERT [28] and ELECTRA [29] models. The Average Micro-F1 >77% shows the efficacy of PIO Detector in detecting the 3 entities: Participants, Intervention, and Outcome. The pre-trained states of these models do not affect the performance after fine-tuning, highlighted by a difference < 1% in the average micro F1-score. PIO Detector is particularly adept in detecting Participants resulting in the highest Recall and Micro-F1 Score among the 3 entities. Due to the highest Average Micro-F1 score among all methods, PubMedBERT [38] was selected for the back-end of the web-based interface of CCS Explorer.

**Case Study.** Fig. 5 shows the Participants, Interventions, and Outcomes detected and their respective scores for the same paper expanded upon in Section III-C for relevance prediction. The paper is titled *Beta-blockers may reduce intrusive thoughts in newly diagnosed cancer patients* by Lindgren et al. [56]. In this paper, participant entities obtain much higher average prediction scores than other entities. The accuracy of participant entity detection across other papers is evident in Table III, where participant entities obtain the highest recall and F1-scores. Overall, the detection of PIO entities across the dataset aligns well with a manual review.

**V. COMPARISON WITH MANUAL EXPLORATION**

The goal of the query used to illustrate the capabilities of CCS Explorer is to answer the following question:
TABLE III: CCS Explorer: Participant, Intervention, Outcome Detection Model Performance

| Model       | Precision | Recall | Micro F1-Score | Average Micro F1-Score |
|-------------|-----------|--------|----------------|------------------------|
|             | Participant | Intervention | Outcome | Participant | Intervention | Outcome | Participant | Intervention | Outcome | P/I/O |
| BioELECTRA [63] | 0.738 | 0.609 | 0.851 | 0.923 | 0.763 | 0.619 | 0.820 | 0.677 | 0.717 | 0.776 |
| PubMedBERT [38] | 0.744 | 0.636 | 0.849 | 0.920 | 0.758 | 0.602 | 0.823 | 0.692 | 0.705 | 0.778 |
| SciBERT [44] | 0.743 | 0.609 | 0.854 | 0.910 | 0.750 | 0.607 | 0.818 | 0.673 | 0.710 | 0.773 |
| BioBERT [37] | 0.743 | 0.635 | 0.853 | 0.915 | 0.765 | 0.591 | 0.809 | 0.687 | 0.700 | 0.771 |
| BluBERT [41] | 0.724 | 0.635 | 0.852 | 0.916 | 0.749 | 0.593 | 0.818 | 0.673 | 0.705 | 0.776 |
| KRISBERT [43] | 0.760 | 0.613 | 0.852 | 0.918 | 0.756 | 0.601 | 0.832 | 0.687 | 0.705 | 0.776 |
| SapBERT [39] | 0.740 | 0.619 | 0.860 | 0.920 | 0.757 | 0.601 | 0.820 | 0.681 | 0.708 | 0.775 |

Objective: A cancer diagnosis provokes significant levels of emotional distress, with intrusive thoughts being the most common manifestation among breast cancer survivors. Cancer-related intrusive thoughts can take the form of emotional memories, flashbacks, nightmares, and intrusive images. Emotional arousal after a severe life stressor prolongs adrenergic activation, which in turn may increase risk for post-traumatic stress symptoms. However, antihypertensive beta-blockers block adrenergic activation and are known to reduce intrusive memories and related psychological distress. Thus, the current study aimed to examine the association between beta-blocker use and the severity of cancer-related intrusive thoughts and related symptoms following a cancer diagnosis.

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Results: Although the high rates of breast-related intrusive thoughts in this sample were similar to those of other studies with recently diagnosed patients, beta-blocker users endorsed 32% fewer intrusive related intrusive thoughts than non-users.

Conclusions: Recently diagnosed cancer patients using beta-blockers reported less cancer-related psychological distress. These results suggest that beta-blocker use may benefit cancer patients undergoing psychological adjustment following diagnosis, and provide a promising direction for future investigations on the pharmacological benefits of beta-blockers for cancer-related distress.

How do anti-hypertensive drugs impact the outcome of colorectal cancer survival? The advanced PubMed query automatically constructed by CCS Explorer shown in Fig. 3 is: "("colorectal" AND (neoplasm OR cancer OR tumor)) OR "colorectal neoplasms" [MeSH] AND ("Adrenergic beta-antagonists" [MeSH] OR "Antihypertensive Agents" [MeSH] OR "beta-blockers") AND ("Cancer Survivors" [MeSH] OR "cancer survivorship" [MeSH] OR "cancer survivors" OR "cancer survival")]. Appropriate query formatting is critical in finding the most relevant clinical cohort studies. The query mentioned earlier returned 11 studies. A more general PubMed query of "colorectal cancer AND hypertension" returned 1,617 results. CCS Explorer automatically formats the anti-hypertensive drug names and all synonymous versions of the outcome "cancer survival" to ensure maximal coverage while still restricting the output to the most relevant studies.

Explicitly comparing CCS Explorer to manual exploration by a trained human curator is enlightening. Even if the human curator appropriately formats the advanced PubMed query, there is still substantial time saving with CCS Explorer. Here, we compared the exploration time after the selection of relevant articles. Based on timings from trained curator studies [15], the average exploration time per relevant article is 29 minutes with a range of 24 to 42 minutes. The variability in manual exploration is based on two factors: the innate skill of the curator and the difficulty of finding the relevant PIO elements in the article based on the article's structure and length. Thus, a trained curator would take 290 minutes on average to explore only 10 relevant articles compared to the 26.32 seconds required by CCS Explorer.

In addition to time savings, CCS Explorer also provides critical context that is not generated during the equivalent manual process. CCS Explorer provides the quantitative relevance rankings of each study. The relevance ranking is beneficial for prioritizing the review of large sets of returned relevant articles. The relevance ranking also helps the curator determine how relevant the results of the advanced PubMed query are to the exploratory objective. CCS Explorer also generates an extractive summary, which takes in only the most relevant sentences from each study. In the demonstrated example, the extractive summary was constructed using the 4 most relevant sentences. However, the user can easily adjust the number of sentences in each extractive summary. The extractive summary allows for fast and efficient exploration by the human curator. Finally, the automated PIO detection and extraction expedites the formation of study inclusion criteria and preliminary curation steps for a subsequent meta-analysis.

VI. CONCLUSION

Recently, there has been an explosion of articles on clinical cohort studies, which are readily available through PubMed. However, the sheer number of articles published daily makes it impossible to read through them to extract relevant information manually. This paper proposes an end-to-end system with a user-friendly graphical interface called CCS Explorer, which makes this accessible to anyone. CCS Explorer
can take a disease as input, generate an advanced query for PubMed, and extract the text from all the resulting articles. Next, it ranks each sentence based on a relevance score, creates an extractive summary of the article along with a summary score, and extracts all Participant, Intervention, and Outcome entities. The Relevance Predictor, Summarizer, and PIO Detector are evaluated quantitatively, and case studies are performed to demonstrate their effectiveness. Thus, CCS Explorer makes the arduous task of performing large-scale meta-analysis and review feasible by drastically reducing the required time and effort.

ACKNOWLEDGMENT

We would like to thank the wonderful team at Morning-side Center for Innovative and Affordable Medicine, Emory University for consultation during the study. This research was funded by National Science Foundation CAREER grant 1944247 to C.M, National Institute of Health grant U19-AG056169 sub-award to C.M., and the McCamish Parkinson’s Disease Innovation Program at Georgia Institute of Technology and Emory University to C.M.

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