A woman with short dark hair, wearing a teal lab coat over a white shirt, is looking down at a computer screen. The screen displays a close-up image of a DNA double helix. She is positioned in front of a window with horizontal blinds. The overall lighting is dim, with a bright light source from the side highlighting her face and the screen.

SHEDDING LIGHT ON CANCER CLINICAL TRIALS: ELIGIBILITY CRITERIA

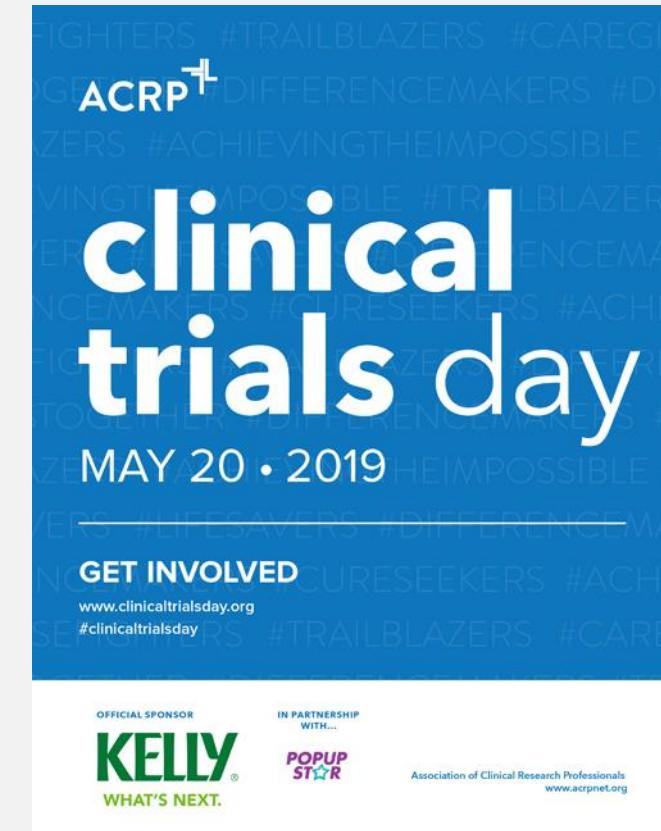
Amritraj Patra

WHAT ARE CLINICAL TRIALS?

Scientific studies conducted to find new/better ways to prevent, screen for, diagnose, or treat disease.

These studies follow strict, scientific standards which protect patients and help produce reliable clinical trial results. Clinical trials are one of the final stages of a long and careful research and development process.

Clinical trials related to drugs are classified into four phases.



#CTD2019

CLINICAL TRIALS PROCESS

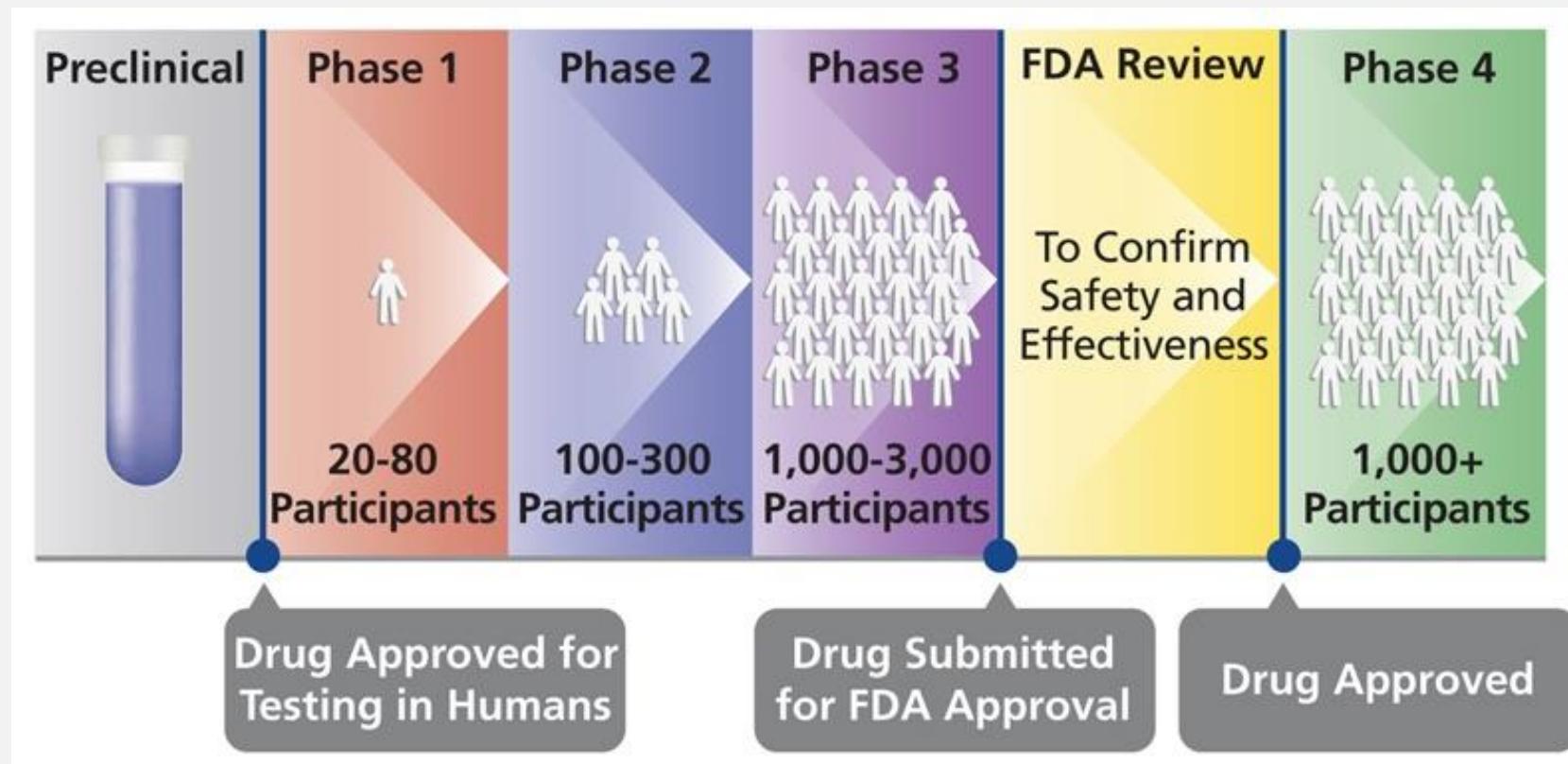


Image source: nih.gov

ELIGIBILITY CRITERIA

Every clinical trial has a protocol or study plan that describes what will be done during the clinical trial, how the clinical trial will be conducted, and why each part of the clinical trial is necessary. The protocol or study plan also includes guidelines called eligibility criteria for who can and cannot participate in the clinical trial.

Criteria often include:

- Age / Gender
- Type or stage of disease
- Medical history
- Current health status



CRITERIA IMPACT ON PATIENT PARTICIPATION

Criteria remain prohibitive for some patient populations:

- 3.7 % included pediatric patients
- 1.7% allowed enrollment of HIV-positive patients with stable disease
- 77 % excluded known, active or symptomatic central nervous system or brain metastases
- 47 % allowed treated or stable brain metastases
- 84.2 % excluded patients with known or active HIV

(Observations from 250 commercial investigational new drug applications for cancer products submitted to the FDA in the year 2015)

“Overly restrictive eligibility criteria may slow patient accrual, limit patients’ access to clinical trials and lead to trial results that don’t fully represent treatment effects in the patient population that will ultimately receive the drug.” -- FDA Commissioner Scott Gottlieb, M.D.
(March 12, 2019)

EXPANDING ELIGIBILITY CRITERIA

Reducing Patient Eligibility Criteria in Cancer Clinical Trials

By Stephen L. George

Purpose: To discuss patient eligibility criteria in phase III cancer clinical trials in the larger setting of the complexity of these trials, to review the various reasons for imposing restrictive eligibility requirements, to discuss the problems caused by these requirements, to argue that these requirements should be greatly relaxed in most cancer clinical trials, to provide some guiding principles and practical suggestions to facilitate such a relaxation, and to give an example of how eligibility requirements were reduced in a recent clinical trial in acute lymphocytic leukemia.

Methods: Implicit and explicit reasons for including eligibility criteria in clinical trials are reviewed. Safety concerns and sample size issues receive special attention. The types of problems restrictive eligibility criteria cause with respect to scientific interpretation, medical

ELIGIBILITY CRITERIA for a clinical trial are patient-specific characteristics that define and limit the class of patients that can be treated on the trial.¹ Phase III clinical trials in cancer have traditionally used restrictive patient eligibility criteria. In some diseases, this practice

applicability, complexity, costs, and patient accrual are described.

Results: A list of three items that each eligibility criterion should meet in order to be included is proposed and applied to a recent trial in acute lymphocytic leukemia.

Conclusion: Phase III clinical trials in cancer should have much broader eligibility criteria than the traditionally restrictive criteria commonly used. Adoption of less restrictive eligibility criteria for most studies would allow broader generalizations, better mimic medical practice, reduce complexity and costs, and permit more rapid accrual without compromising patient safety or requiring major increases in sample size.

J Clin Oncol 14:1364-1370. © 1996 by American Society of Clinical Oncology.

clinical trials. Despite the repeated and widely publicized arguments reported by Yusef et al³ and Peto et al⁴ in favor of large simple trials, most phase III cancer clinical trials are relatively small (by the standards of size in other diseases) and complex. It is not the purpose of this report

United States Senate
WASHINGTON, DC 20510

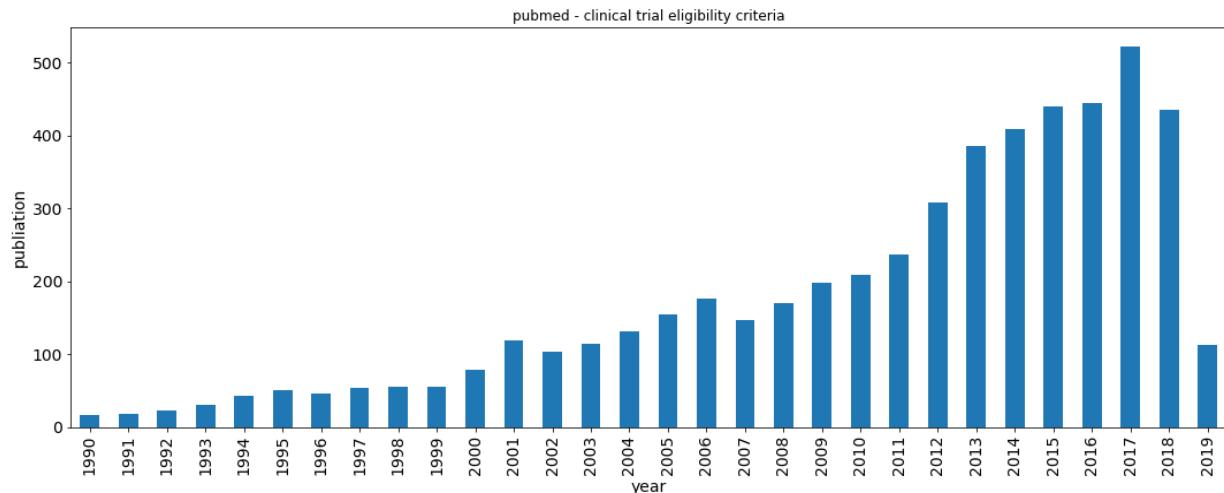
October 12, 2018

Francis S. Collins, M.D., Ph.D.
Director
National Institutes of Health
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Director Collins:

As the National Institutes of Health (NIH) conducts regular review of policy and guidelines related to grant applications, we request that existing guidance be updated to ensure eligibility criteria for clinical trials are not disproportionately excluding racial and ethnic minority groups from participation. We are encouraged by NIH's work to support research that seeks to reduce and eliminate health disparities. Specific guidance for the application and review process on recognizing when research protocols create unintentional barriers to participation will further strengthen NIH's policy and mission of inclusive enrollment of minorities in NIH-funded clinical research.

DATA SOURCE IDENTIFICATION FOR CLINICAL TRIAL ELIGIBILITY CRITERIA RESOLUTION



Contents lists available at ScienceDirect
Journal of Biomedical Informatics

journal homepage: www.elsevier.com/locate/yjbin

Unsupervised mining of frequent tags for clinical eligibility text indexing

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ABSTRACT

Clinical text, such as clinical trial eligibility criteria, is largely underused in state-of-the-art medical search engines due to difficulties of accurate parsing. This paper proposes a novel methodology to derive a semantic index for clinical eligibility documents based on a controlled vocabulary of frequent tags, which are automatically mined from the text. We applied this method to eligibility criteria on ClinicalTrials.gov and report that frequent tags (1) define an effective and efficient index of clinical trials and (2) are unlikely to grow radically when the repository increases. We proposed to apply the semantic index to filter clinical trial search results and we concluded that frequent tags reduce the result space more efficiently than an uncontrolled set of UMLS concepts. Overall, unsupervised mining of frequent tags from clinical text leads to an effective semantic index for the clinical eligibility documents and promotes their computational reuse.

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Article

Learning Eligibility in Cancer Clinical Trials Using Deep Neural Networks

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Abstract: Interventional cancer clinical trials are generally too restrictive, and some patients are often excluded on the basis of comorbidity, past or concomitant treatments, or the fact that they are over a certain age. The efficacy and safety of new treatments for patients with these characteristics are, therefore, not defined. In this work, we built a model to automatically predict whether short clinical statements were considered inclusion or exclusion criteria. We used protocols from cancer clinical trials that were available in public registries from the last 18 years to train word-embeddings, and we constructed a dataset of 6M short free-texts labeled as eligible or not eligible. A text classifier was trained using deep neural networks, with pre-trained word-embeddings as inputs, to predict whether or not short free-text statements describing clinical information were considered eligible. We additionally analyzed the semantic reasoning of the word-embedding representations obtained and were able to identify equivalent treatments for a type of tumor analogous with the drugs used to treat other tumors. We show that representation learning using deep neural networks can be successfully leveraged to extract the medical knowledge from clinical trial protocols for potentially assisting practitioners when prescribing treatments.

Keywords: clinical trials; clinical decision support system; natural language processing; word embeddings; deep neural networks

CLINICAL TRIAL TEXT ANALYSIS

S. National Library of Medicine
[ClinicalTrials.gov](#)

ClinicalTrials.gov is a database of studies from around the world.

There are 305,352 research studies in the United States and in 209 countries.

ClinicalTrials.gov is a resource provided by the National Library of Medicine.

NOTE: Listing a study does not mean it has been evaluated by the U.S. Federal Government. See the [disclaimer](#) for details.

If you are considering participating in a study, talk to your health care provider and learn about the [risks and benefits](#).

56284 Studies found for: **Interventional Studies | Cancer**
Also searched for **Neoplasm** and **Tumor**. [See Search Details](#)

Applied Filters: **Interventional**

List By Topic On Map Search Details

Hide Filters

Download Subscribe to RSS

Show/Hide Columns

Showing: 1-10 of 56,284 studies 10 studies per page

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Recruiting	Development of an Intervention to Enhance Cancer Pain Management	• Other Cancer	• Behavioral: Enhancing Cancer Pain Management	• Massachusetts General Hospital Cancer Center Boston, Massachusetts, United States
2	<input type="checkbox"/>	Not yet recruiting	Imaging With [11C]Martinostat in Breast Cancer	• Breast Cancer	• Drug: [11C]Martinostat • Device: MR-PET scanner	• Massachusetts General Hospital Cancer Center Boston, Massachusetts, United States
3	<input type="checkbox"/>	Recruiting	Testing Feasibility of Motivational Interviewing for Patient-Reported Cancer Pain Goals	• Other Cancer	• Behavioral: Motivational Interviewing	• Dana Farber Cancer Institute Boston, Massachusetts, United States
4	<input type="checkbox"/>	Recruiting	Rehabilitation After Breast Cancer	• Breast Cancer	• Behavioral: Individually	• Rigshospitalet

[View All Results](#)

VIEW OF A FILE

```
<?xml version="1.0" encoding="ISO-8859-1"?>
```

```
<clinical_study rank="1643">
```

```
    <!-- This xml conforms to an XML Schema at:
```

```
--<description>
```

HYCAMTIN at a dose of 2.0 mg/m² on Days 1 and 8 every 21 days followed by carboplatin at AUC 5 on Day 1

```
</description>
```

```
<arm_group_label>Single-arm</arm_group_label>
```

```
</intervention>
```

```
--<eligibility>
```

```
--<criteria>
```

```
--<textblock>
```

Inclusion criteria: - Subject must have baseline laboratory values as follows: - Hemoglobin 9.0 g/dL - Neutrophils 1,500/mm³ - Platelets 100,000/mm³ - Creatinine 1.5 mg/dL (133 mol/l) or creatinine clearance 60 mL/min - Serum bilirubin < 2.0 mg/dL (< 35 umol/L) - SGOT/AST, SGPT/ALT and alkaline phosphatase < 2 times ULN if liver metastases are absent by abdominal CT or MRI or < 5 times ULN if liver metastases are present - Subject is allowed to have received, but is not required to have received, one additional prior non-cytotoxic regimen for management of recurrent or persistent disease according to the following definition: Non-cytotoxic (biologic or cytostatic) agents include (but are not limited to) monoclonal antibodies, cytokines, and small-molecule inhibitors of signal transduction - Subject is female 18 years of age with an ECOG Performance Status of 0, 1 or 2 - Subject has recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer which was histologically confirmed at the time of the primary diagnosis - Subject has received one prior platinum-based chemotherapeutic regimen (containing either carboplatin or cisplatin) for the treatment of primary disease. Consolidation chemotherapy is not permitted - Subject's disease is considered potentially platinum-sensitive (i.e., have had a platinum-free interval following complete response to carboplatin or cisplatin of greater than 6 months) - Subject must have at least one measurable lesion as determined by diagnostic studies including CT or MRI or physical exam. Measurable disease must be accurately measured in at least one dimension (longest dimension to be recorded). Each lesion must be 20 mm in their longest dimension when measured by conventional techniques, including palpation, plain X-ray, CT and MRI, or 10 mm when measured by spiral CT. Palpable tumor masses that cannot be evaluated radiologically must have 2 diameters 20 mm. An attempt to document lesion size by ultrasound should be undertaken for palpable lesions not visualized on CT (or MRI). - The same diagnostic imaging method used to evaluate disease must be used throughout the study to evaluate lesions consistently - Stable blood, liver and renal functions. - Subjects of child-bearing potential must be practicing adequate contraception (e.g. oral contraceptives, diaphragm plus spermicide, or IUD) for at least 3 months prior to study start. The same contraceptive method should be used throughout the study and continue for at least 4 weeks after the end of the study Exclusion criteria: - Pregnant or lactating. - Subject has received more than 1 prior chemotherapy regimen or a history of consolidation cytotoxic chemotherapy - Subject has concomitant or history of previous malignancies, with the exception of adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, or other cancer from which the subject has been disease-free for 5 years - Subject has brain metastases as documented by CT or MRI. Note: Asymptomatic subjects do not require CT or MRI to rule out brain metastases - Received previous treatment with HYCAMTIN. - Subject has received an investigational agent within 30 days or 5 half-lives (whichever is longer) prior to study entry - Received prior radiation therapy for ovarian cancer

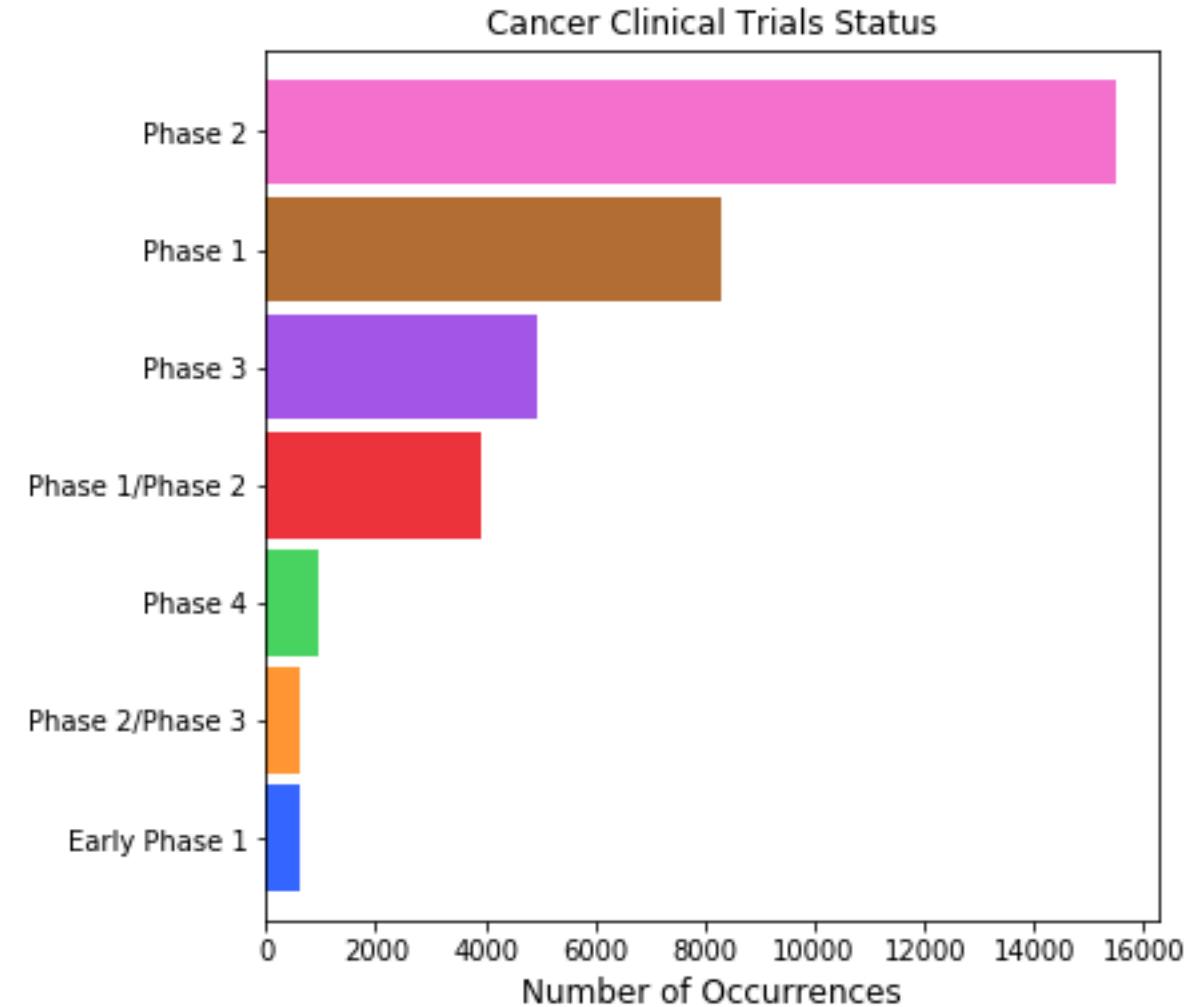
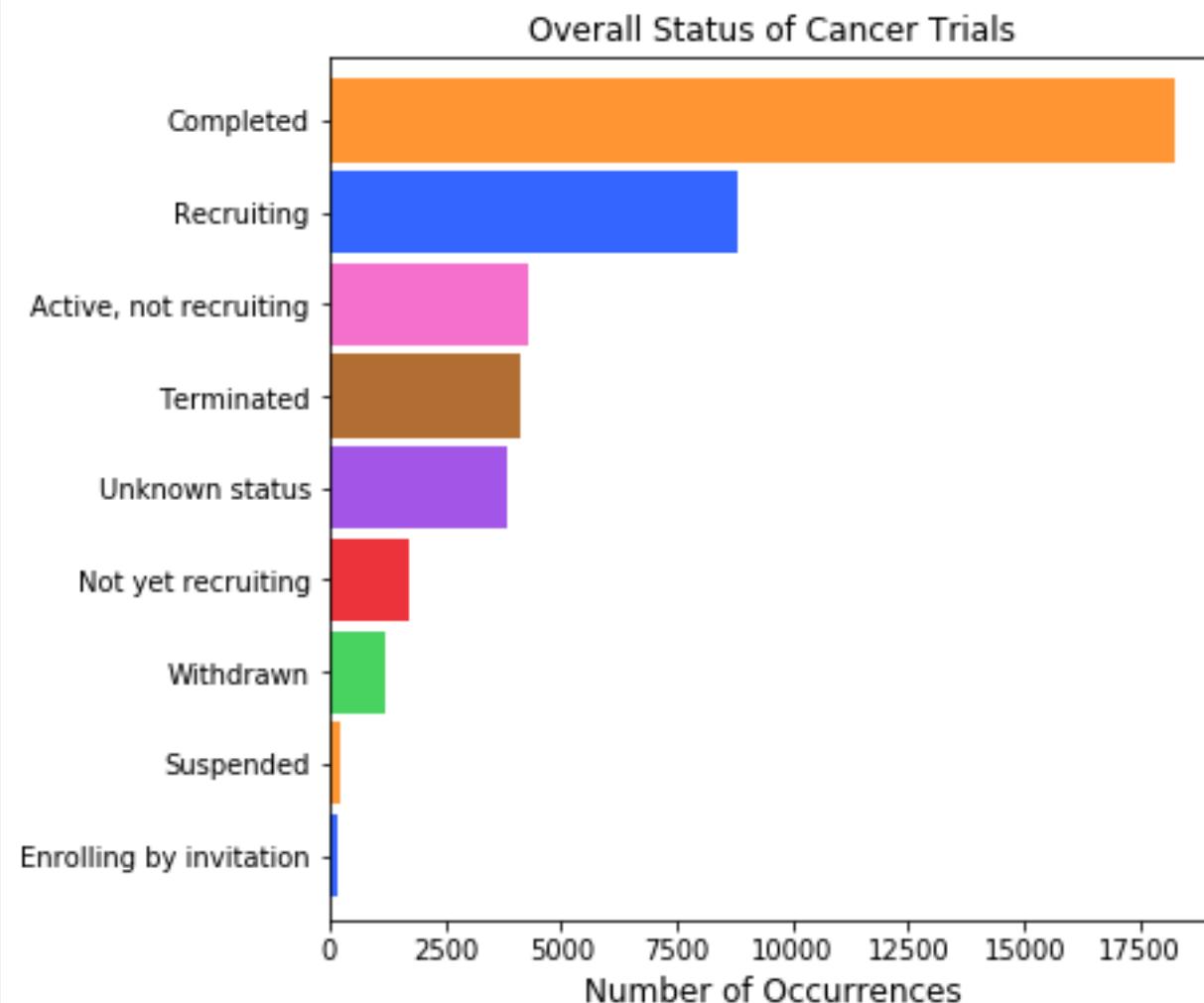
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</textblock>
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</criteria>
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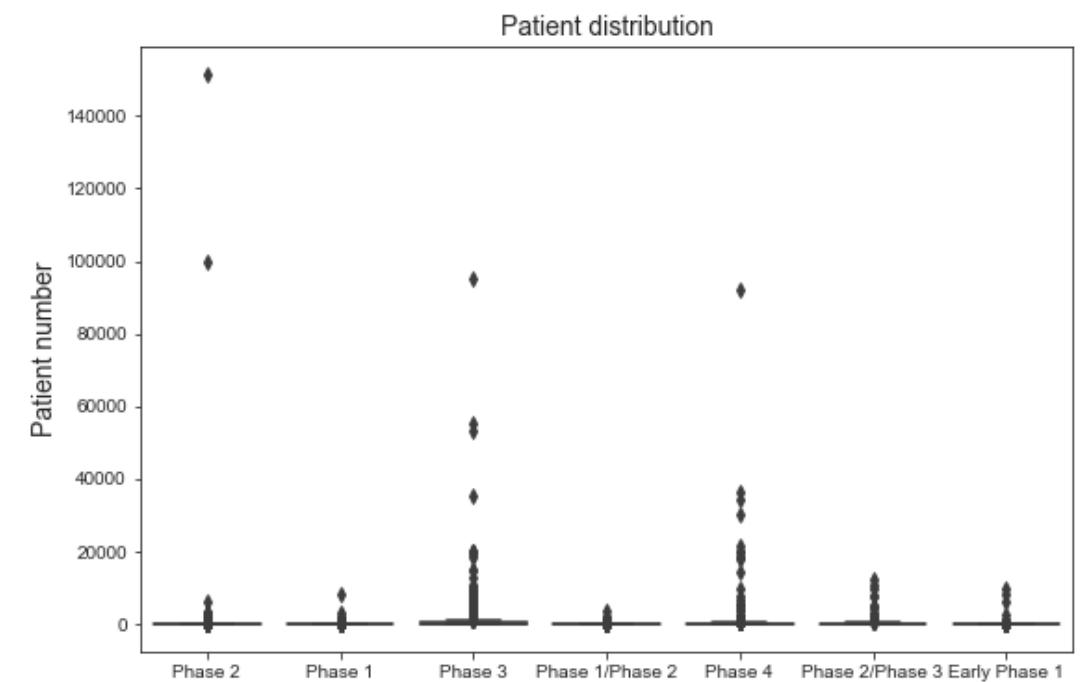
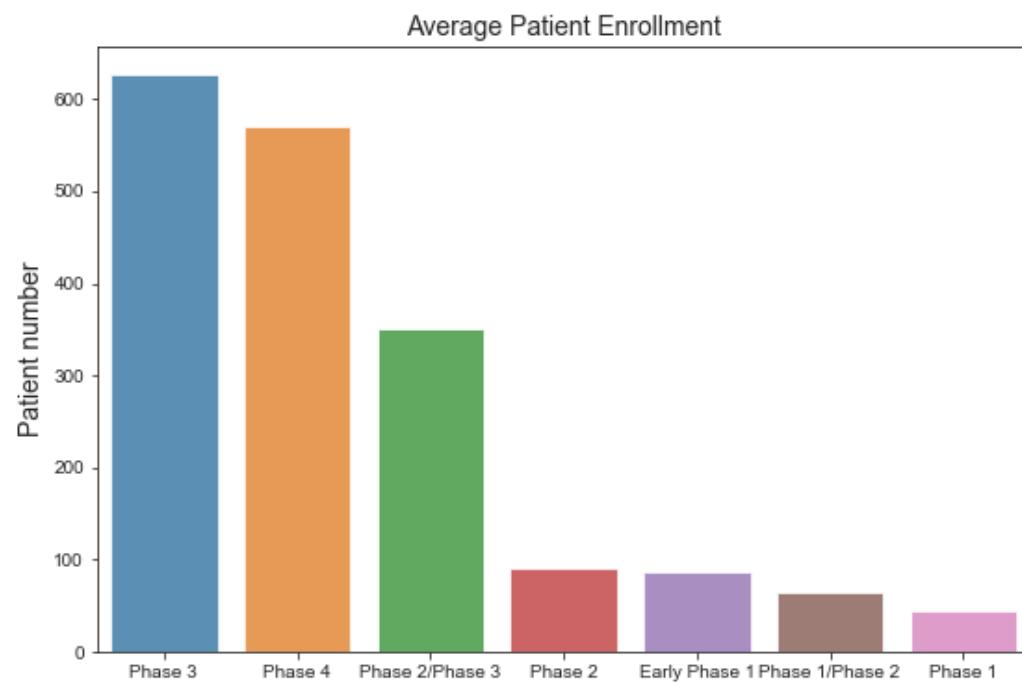
```
<gender>Female</gender>
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```
<minimum_age>18 Years</minimum_age>
```

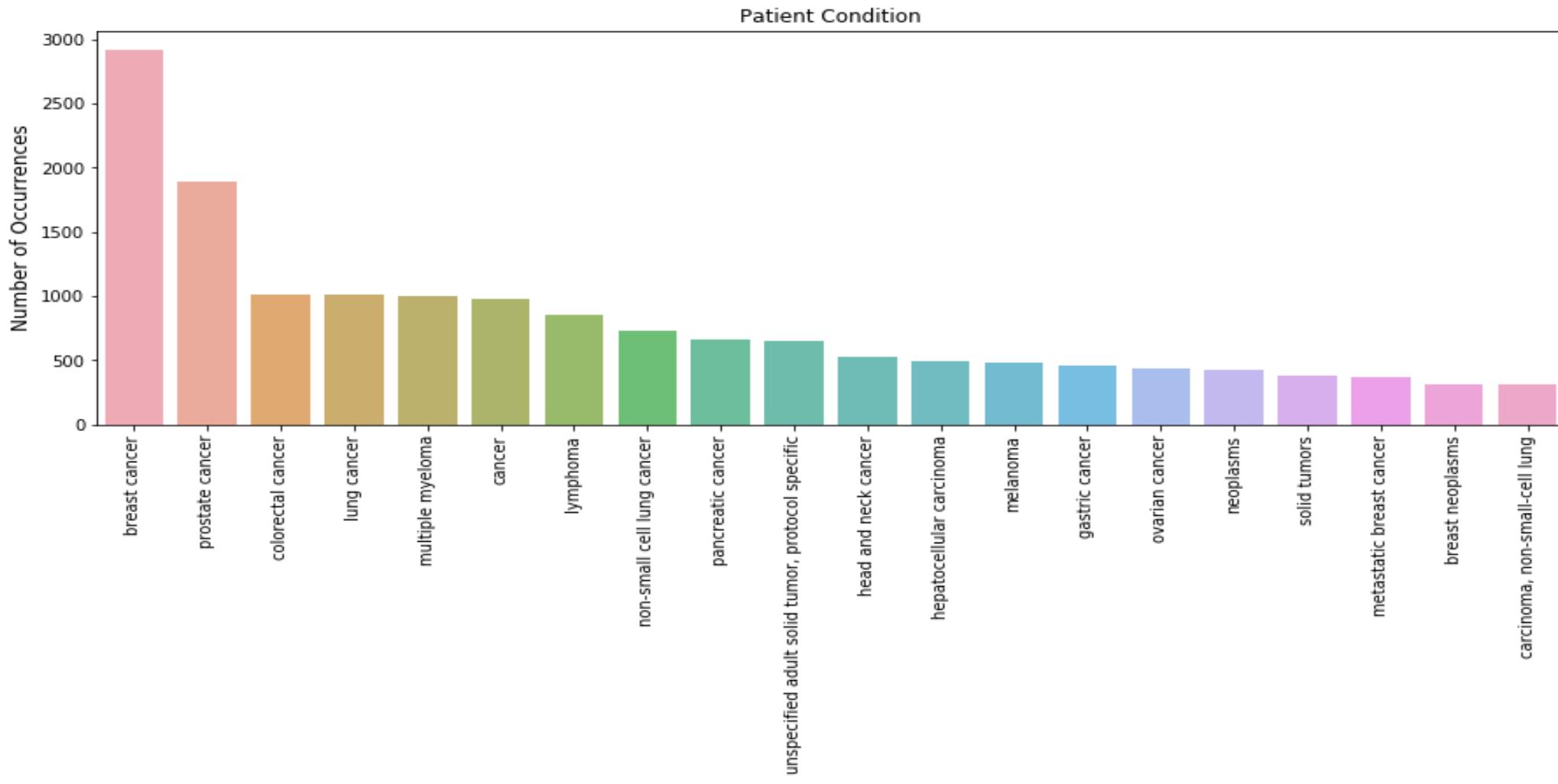
DATA EXPLORATION



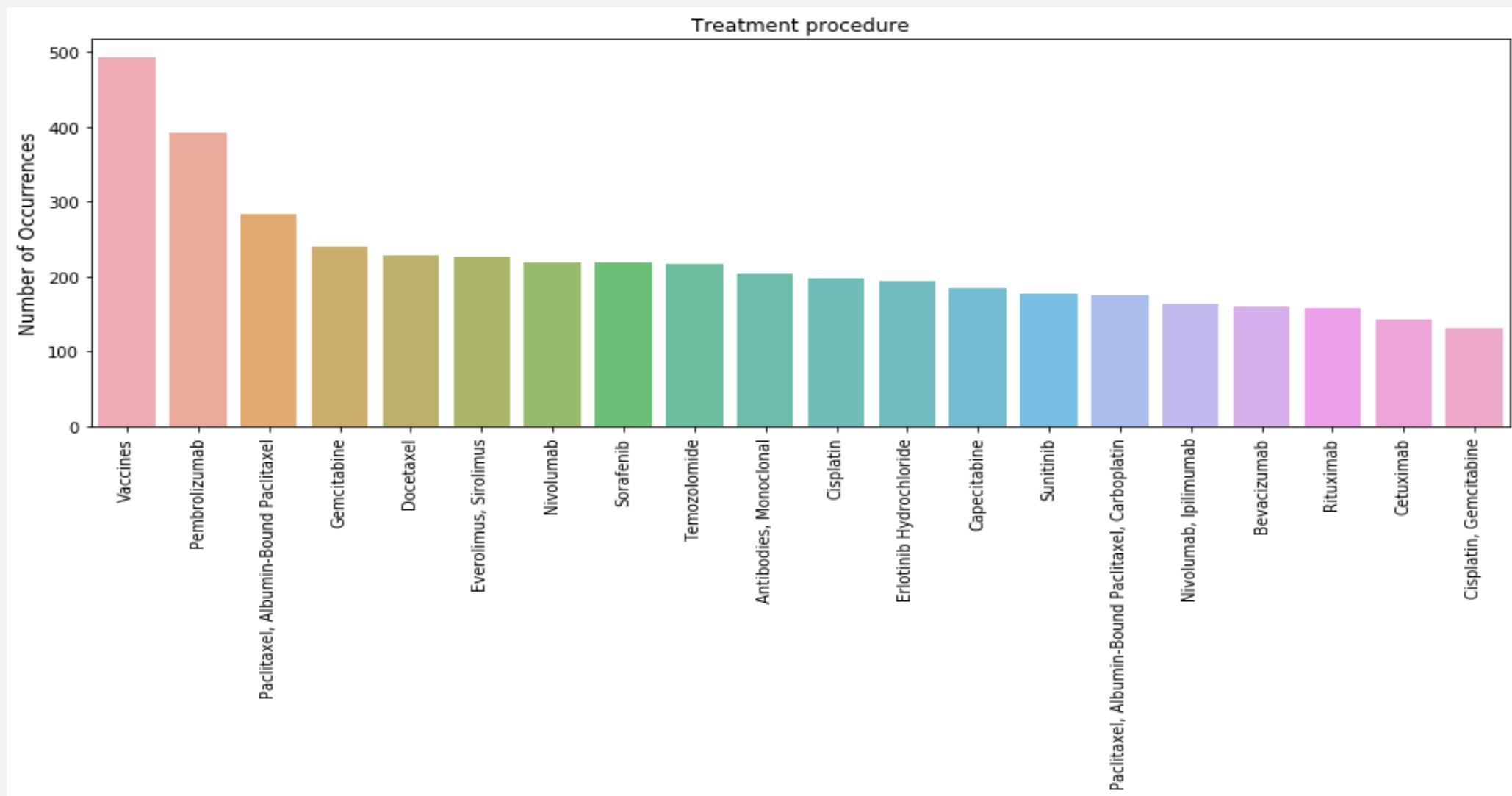
PATIENT ENROLLMENT IN DIFFERENT PHASES OF TRIAL



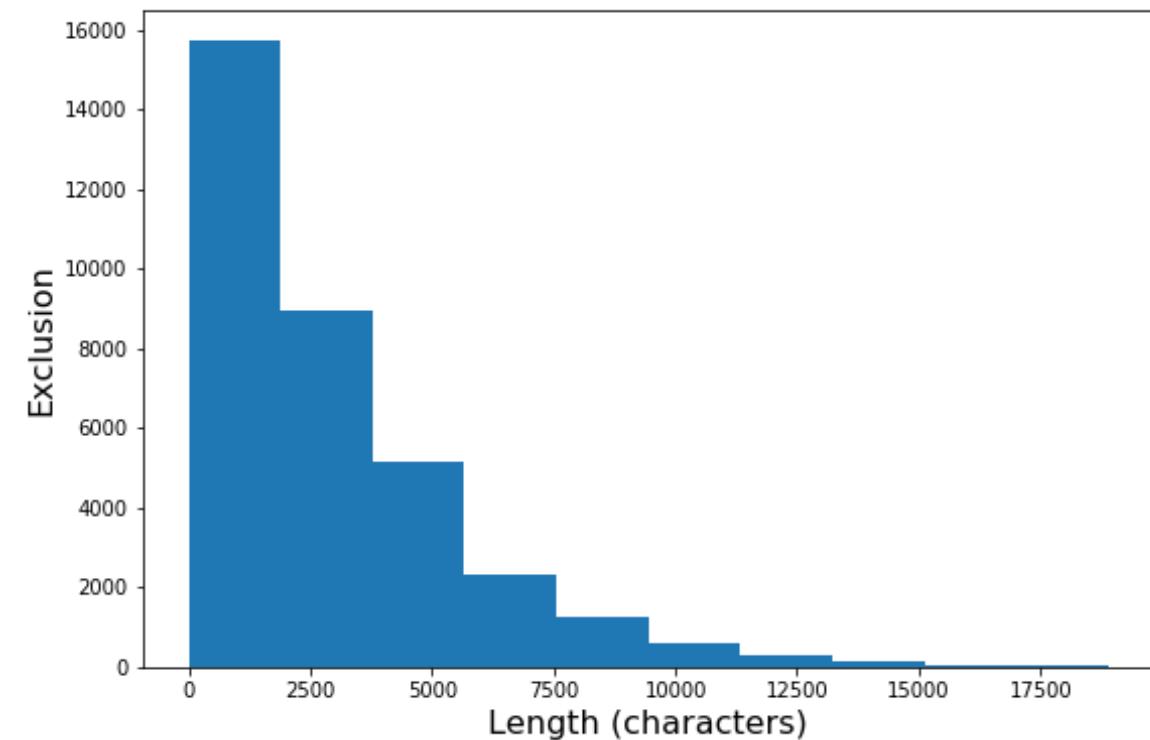
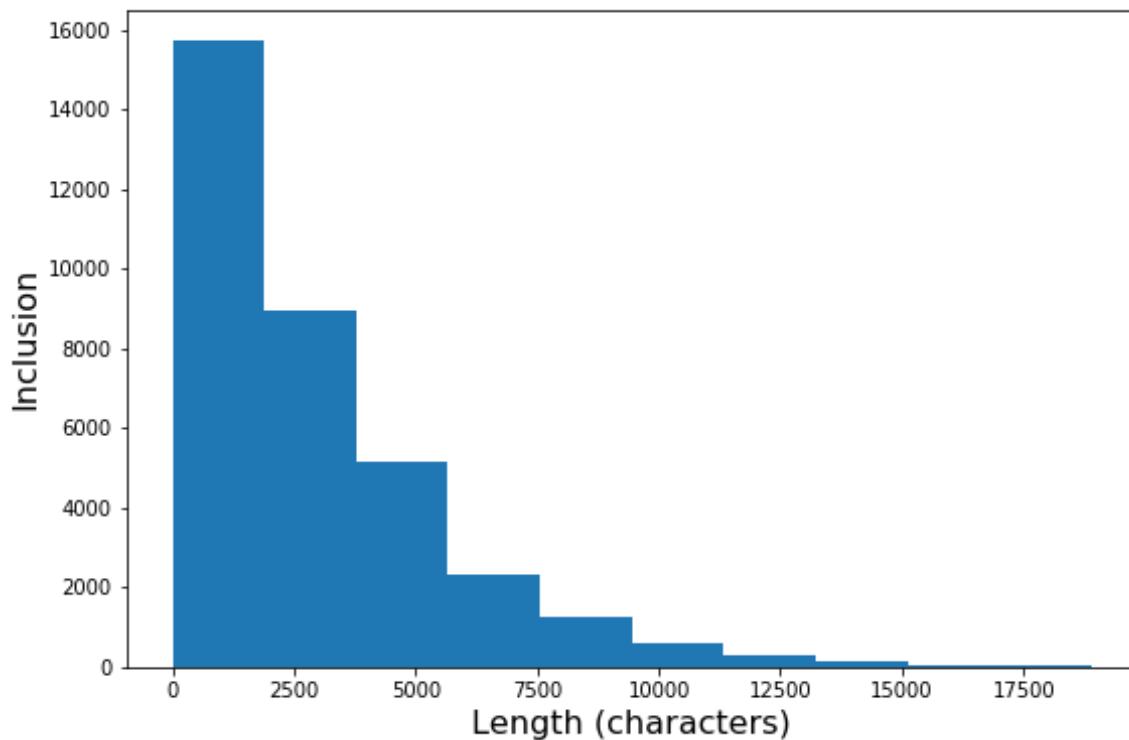
TOP CANCER CONDITION UNDERGOING TRIAL



TOP CANCER TREATMENT PROCEDURES



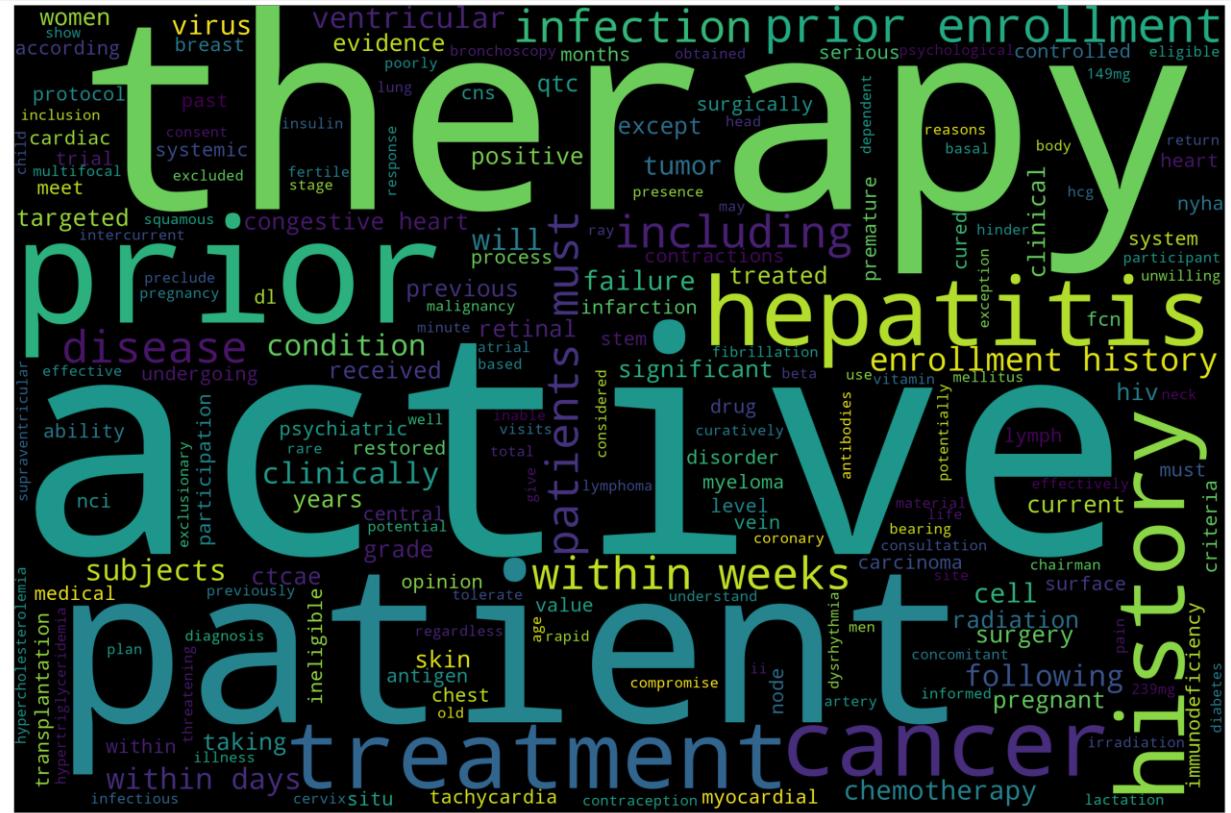
TRIAL INCLUSION/EXCLUSION CRITERIA



Inclusion
Exclusion

34494 non-null object
34494 non-null object

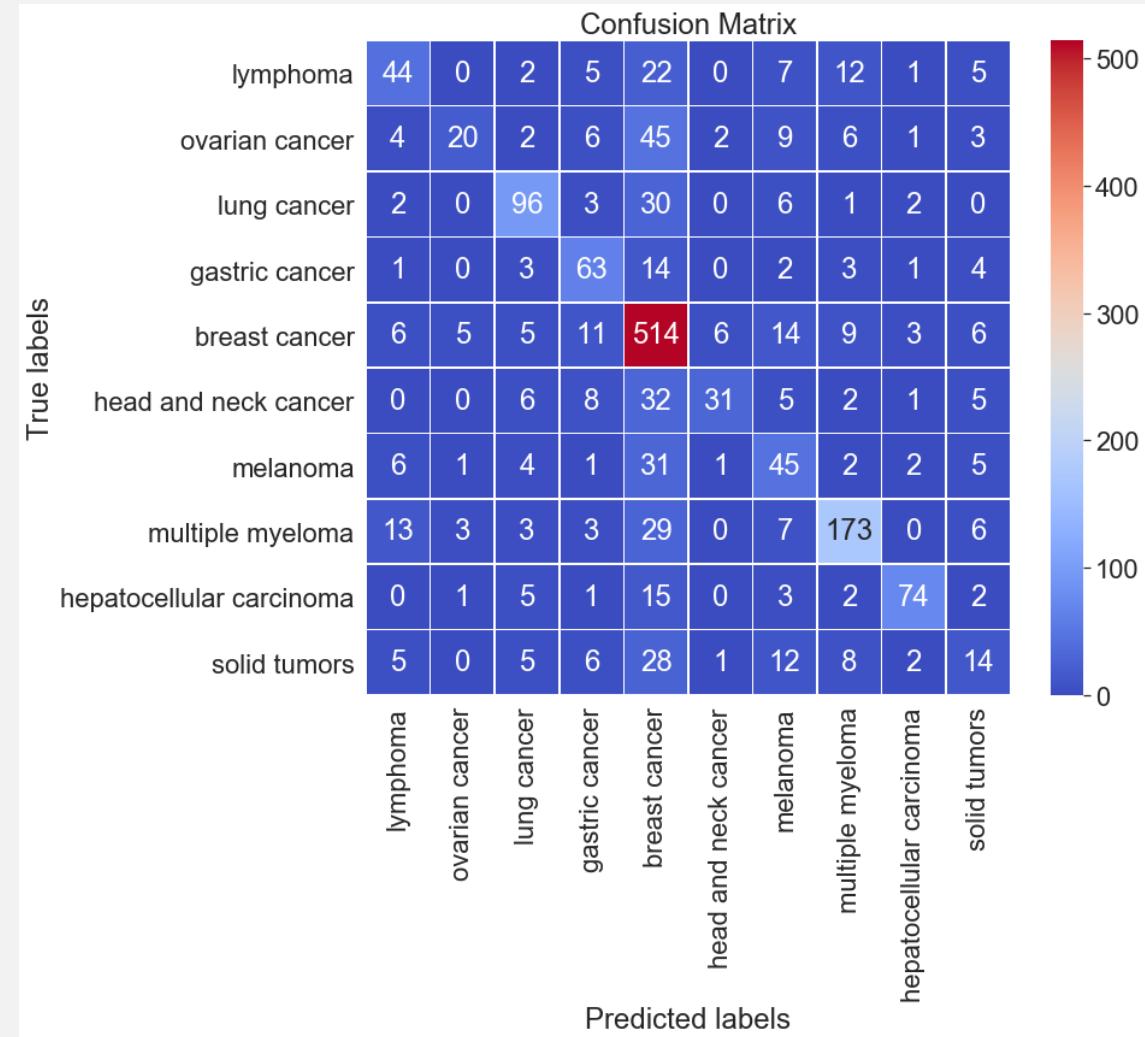
WORD CLOUD OF INCLUSION/EXCLUSION CRITERIA



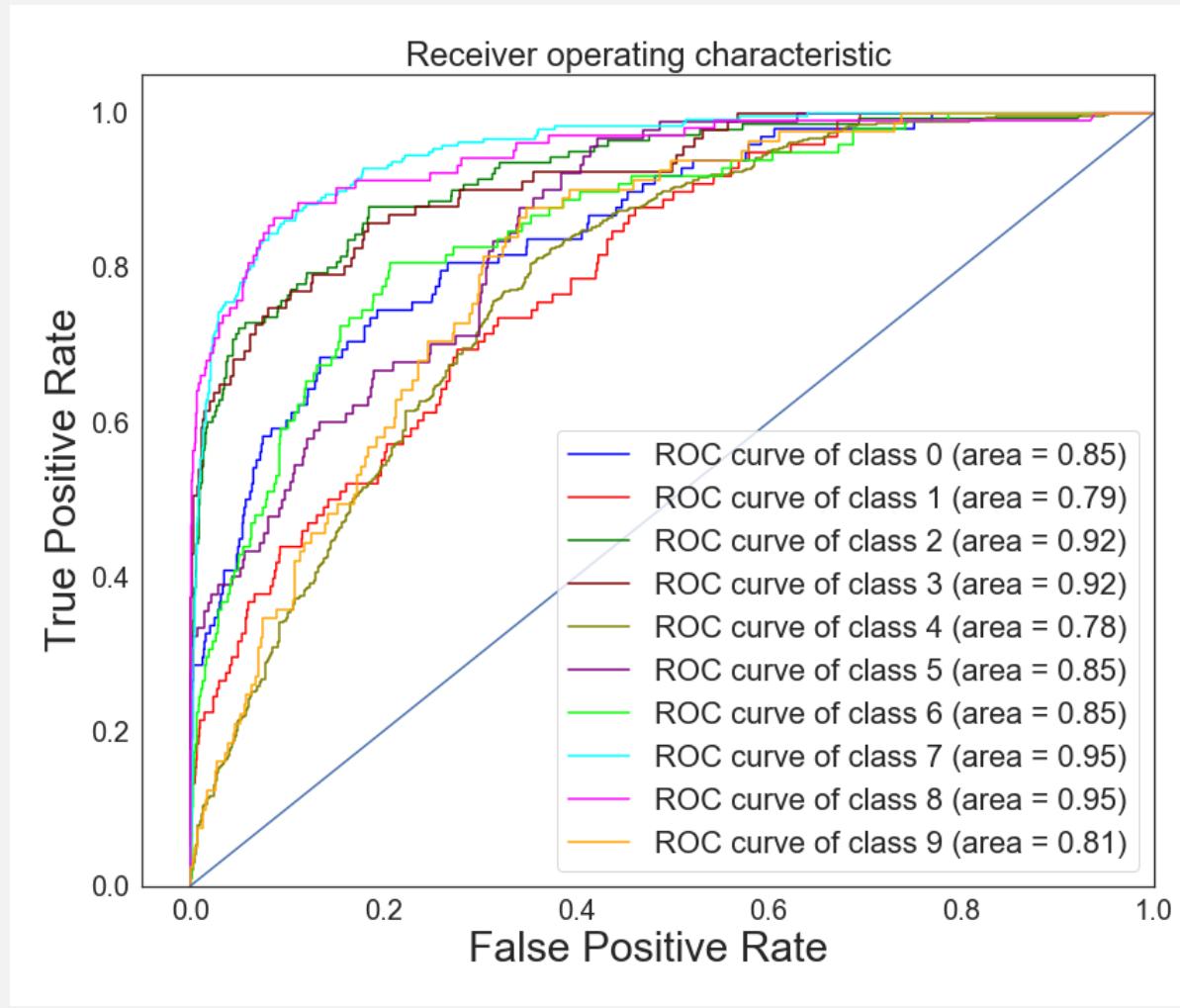
PREDICTING CANCER CONDITIONS FROM INCLUSION/EXCLUSION CRITERIA

Accuracy: 0.665

	precision	recall	f1-score	support
0	0.54	0.45	0.49	98
1	0.67	0.20	0.31	98
2	0.73	0.69	0.71	140
3	0.59	0.69	0.64	91
4	0.68	0.89	0.77	579
5	0.76	0.34	0.47	90
6	0.41	0.46	0.43	98
7	0.79	0.73	0.76	237
8	0.85	0.72	0.78	103
9	0.28	0.17	0.21	81



ROC CURVE FOR CANCER CONDITIONS



THANK YOU



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Biomedical Scientist



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