medExtractR_tapering Vignette

2022-06-06

Introduction

The medExtractR package uses a natural language processing (NLP) system called medExtractR.¹ This system is a medication extraction system that uses regular expressions and rule-based approaches to identify key dosing information including drug name, strength, dose amount, frequency or intake time, dose change, and last dose time. In this vignette, we introduce the medExtractR_tapering function, an extension on the basic medExtractR function. The goal of this function is to extract more information for drugs following a tapering schedule. Some drugs (e.g., steroids, antidepressants) require weaning schedules to be gradually stopped in order to avoid adverse side effects or withdrawal symptoms. Tapering schedules are much more complex and require more entities in order to build longitudinal dose data.

Tapering extension to medExtractR

Similar to medExtractR's extract_entities subfunction, the tapering extension has its own corresponding subfunction called extract_entities_tapering. In addition to the entities identified by the basic medExtractR function, the tapering extension can also identify: dispense amount (entity name in output: "DispenseAmt"); number of refills ("Refill"); keywords indicating a particular dose schedule pattern, such as "taper", "wean", "dose pack", or "discontinue" ("DoseSchedule"); keywords indicating whether a dose is past, current, or future ("TimeKeyword"); words or symbols linking consecutive doses in a tapering schedule ("Transition"); and prepositions adjacent to other entities ("Preposition"), used in some contexts to preserve or infer meaning.

library(medExtractR)

This extended function was created to handle three common patterns of dosing found in notes for patients being treated with medications that commonly use a tapering schedule to gradually decrease the patient's dose. The drug prednisone is an example of one such medication, and de-identified notes for patients being treated with prednisone were used during medExtractR_tapering development (described in a later section).

We call these additional dosing patterns "taper I", "taper II", and "alternating" schedules. In the subsections below, we explain the structure of each of these schedules and present an example of medExtractR_tapering being applied to each.

$Taper \ I$

Taper I schedules are tapering regimens in which consecutive doses are explicitly written out. Examples of taper I schedules include:

- "prednisone 10 mg tablet 4 tablets by mouth daily for 2 weeks then 3 tablets by mouth daily for 1 week then 2 tablets by mouth daily for 1 week then 1.5 tablets by mouth daily for 1 week then 1 tablet by mouth daily for 1 week then 0.5 tablet by mouth daily for 1 week"
- "will increase prednisone to 15 mg once a day for 5-7 days, then taper (10 mg to 5 mg to off) over 2 weeks"
- "prednisone 5 mg daily for 7 days and 2.5 mg daily for another 3 days"

In a taper I schedule, at least some dose information is available for two or more segments of a weaning schedule. In the first example above, the strength of an individual tablet is provided up front, and each segment of the taper schedule just provides the number of tablets to take. This represents an ideal case where a clear duration is available for each segment. In the second example, the durations associated with each segment are less clear. MedExtractR only identifies the information exactly as it's written in a note, but a post-processing function could determine how to assign daily dosages given this information (e.g., 15 mg for 6 days, 10 mg for 7 days, 5 mg for 7 days, 0 mg).

Taper 1 schedule

subset(pred_mxr, filename == sub(".+/", "", pred_fn[1]))

##		filename	entity	expr	pos
##	1	predpid1_2013-04-27_note1_1.txt	DrugName	prednisone	561:571
##	2	predpid1_2013-04-27_note1_1.txt	Strength	-	572:577
##	3	predpid1_2013-04-27_note1_1.txt	DoseAmt	4	585:586
##	4	predpid1_2013-04-27_note1_1.txt	Route	by mouth	595:603
##	5	predpid1_2013-04-27_note1_1.txt	Frequency	daily	604:609
##	6	predpid1_2013-04-27_note1_1.txt	Preposition	for	610:613
##	7	predpid1_2013-04-27_note1_1.txt	Duration	2 weeks	614:621
##	8	predpid1_2013-04-27_note1_1.txt	Transition	then	622:626
##	9	$predpid1_2013-04-27_note1_1.txt$	DoseAmt	3	627:628
##	10	$predpid1_2013-04-27_note1_1.txt$	Route	by mouth	637:645
##	11	$\tt predpid1_2013-04-27_note1_1.txt$	Frequency	daily	646:651
##	12	$\tt predpid1_2013-04-27_note1_1.txt$	Preposition	for	652:655
##	13	$\tt predpid1_2013-04-27_note1_1.txt$	Duration	1 week	656:662
##	14	$\tt predpid1_2013-04-27_note1_1.txt$	Transition	then	663:667
##	15	$\tt predpid1_2013-04-27_note1_1.txt$	DoseAmt	2	668:669
##	16	$\tt predpid1_2013-04-27_note1_1.txt$	Route	by mouth	678:686
##	17	$\tt predpid1_2013-04-27_note1_1.txt$	Frequency	daily	687:692
##	18	$\tt predpid1_2013-04-27_note1_1.txt$	${\tt Preposition}$	for	693:696
##	19	$\tt predpid1_2013-04-27_note1_1.txt$	Duration	1 week	697:703
##	20	$\tt predpid1_2013-04-27_note1_1.txt$	Transition	then	704:708
##	21	$\tt predpid1_2013-04-27_note1_1.txt$	DoseAmt	1.5	709:712
##	22	$\tt predpid1_2013-04-27_note1_1.txt$	Route	by mouth	721:729
		$\tt predpid1_2013-04-27_note1_1.txt$	Frequency	daily	730:735
##	24	$\tt predpid1_2013-04-27_note1_1.txt$	${\tt Preposition}$	for	736:739
##	25	$\tt predpid1_2013-04-27_note1_1.txt$	Duration	1 week	740:746
		$\tt predpid1_2013-04-27_note1_1.txt$	Transition	then	747:751
##	27	$\tt predpid1_2013-04-27_note1_1.txt$	DoseAmt	1	752:753
##	28	predpid1_2013-04-27_note1_1.txt	Route	by mouth	761:769

```
## 29 predpid1_2013-04-27_note1_1.txt
                                         Frequency
                                                        daily 770:775
## 30 predpid1_2013-04-27_note1_1.txt Preposition
                                                          for 776:779
## 31 predpid1 2013-04-27 note1 1.txt
                                          Duration
                                                       1 week 780:786
## 32 predpid1_2013-04-27_note1_1.txt
                                        Transition
                                                         then 787:791
## 33 predpid1_2013-04-27_note1_1.txt
                                           DoseAmt
                                                          0.5 792:795
## 34 predpid1 2013-04-27 note1 1.txt
                                             Route
                                                     by mouth 803:811
## 35 predpid1 2013-04-27 note1 1.txt
                                         Frequency
                                                        daily 812:817
## 36 predpid1_2013-04-27_note1_1.txt Preposition
                                                          for 818:821
## 37 predpid1_2013-04-27_note1_1.txt
                                          Duration
                                                       1 week 822:828
```

Taper II

Taper II schedules are tapering regimens in which a repetitive dosing change is written more concisely. Typically, this is written in the form of "change by at". As an example, consider the phrase "Take prednisone 5mg tablet 4 tabs daily for one week, then decrease by 5mg every week then stop" In this excerpt, the patient's initial dose is 20 mg per day for a duration of one week. From the second part of the phrase, we can infer that after the first week, the patient's dosage will be 15 mg daily for the second week, 10 mg daily for the third week, 5 mg daily for the fourth week, and then 0 mg (off) after that.

```
# Taper 2 schedule
```

```
subset(pred_mxr, filename == sub(".+/", "", pred_fn[2]))
```

##		filename	entity	expr	pos
##	38	predpid2_2015-12-11_note1_1.txt	DrugName	prednisone	474:484
##	39	predpid2_2015-12-11_note1_1.txt	Strength	5 mg	485:489
##	40	predpid2_2015-12-11_note1_1.txt	DoseStrength	20mg	502:506
##	41	$\tt predpid2_2015-12-11_note1_1.txt$	IntakeTime	every morning	507:520
##	42	$\tt predpid2_2015-12-11_note1_1.txt$	Preposition	for	521:524
##	43	$\tt predpid2_2015-12-11_note1_1.txt$	Duration	14 days	525:532
##	44	$\tt predpid2_2015-12-11_note1_1.txt$	Transition	then	533:537
##	45	$\tt predpid2_2015-12-11_note1_1.txt$	DoseChange	decrease	538:546
##	46	$\tt predpid2_2015-12-11_note1_1.txt$	Preposition	by	547:549
##	47	$\tt predpid2_2015-12-11_note1_1.txt$	DoseStrength	5 mg	550:554
##	48	$\tt predpid2_2015-12-11_note1_1.txt$	Duration	every 7 days	555:567
##	49	predpid2_2015-12-11_note1_1.txt	Preposition	until	568:573
##	50	$\tt predpid2_2015-12-11_note1_1.txt$	DoseSchedule	done	574:578

Alternating

Alternating schedule

Alternating schedules consist of a patient being on multiple doses (typically two), with different dosages on consecutive days. The patient may have two specific doses, for example "20mg of prednisone on even days and 10mg of prednisone on odd days", or they may be on a single dose but taking it intermittently, for example "take prednisone 5mg tablet every other day for one week".

```
subset(pred_mxr, filename == sub(".+/", "", pred_fn[3]))
##
                             filename
                                             entity
                                                               expr
                                                                        pos
## 51 predpid3_2017-01-01_note1_1.txt
                                           DrugName
                                                               pred 630:634
## 52 predpid3_2017-01-01_note1_1.txt DoseStrength
                                                             2.5 mg 635:641
## 53 predpid3_2017-01-01_note1_1.txt
                                              Route
                                                             orally 642:648
## 54 predpid3_2017-01-01_note1_1.txt
                                          Frequency every other day 649:664
## 55 predpid3 2017-01-01 note1 1.txt DoseSchedule
                                                          alternate 665:674
## 56 predpid3_2017-01-01_note1_1.txt
                                       Preposition
                                                               with 675:679
## 57 predpid3_2017-01-01_note1_1.txt DoseStrength
                                                               5 mg 680:684
## 58 predpid3_2017-01-01_note1_1.txt
                                          Frequency every other day 685:700
```

Note: It is possible for a dosing regimen to be written in a mixture of these cases. For example, the phrase

"restart pred at 40 mg daily for 1 week, 30 mg daily for one week, 20 mg daily for one week and then drop by 5 mg per week after that" starts as a taper I schedule, but ends as a taper II schedule. An individual segment of a taper I schedule could also involve an alternating dose, particularly taking a single dose every other day in weaning schedules.

medExtractR_tapering development

The tapering extension to medExtractR was developed on a set of 162 training notes from Vanderbilt University's de-identified EHR system, the Synthetic Derivative (SD). As a first step, we developed annotation guidelines as a way to rigorously define the definition of each new entity (or changes to any existing entity, if applicable). Two reviewers would then independently annotate each note, and a third party group would help resolve any discrepancies. The annotation guidelines were then updated, and annotations were revised, based on this process.

This set of training notes was also used to generate the default entity dictionaries included within the medExtractR package. The annotations, which serve as the gold standard for what information should be extracted, were used as the starting point for all dictionaries. Those expressions were then removed (e.g., mispelled words) or generalized using regular expressions (e.g., changing a "2 days" duration to "\d{1,2} days", where \d represents any one or two digit number). Examples of some expressions in the new entity dictionaries are provided below:

- Duration: much of the duration dictionary is written using regular expressions to account for various numbers being used. Examples of expressions that would be considered durations are: 2 weeks, next 3 days, 1 week ago, weekly, day five, and dates (for example, to capture expressions like "Remain on prednisone 5mg daily until April 15").
- DoseSchedule: words indicating a specific dosing schedule (taper, weaning, dose pack, etc.) or stopping keywords (off, stop, discontinue, etc.)
- TimeKeyword: was taking, yesterday, remain, tomorrow, current, etc.
- Transition: then, followed by, and punctuation such as ; or ,.
- Preposition: from, of, by, on, to, at, etc. If a preposition is part of an expression for another entity (e.g., "by" in "by mouth"), then it is not extracted separately as a preposition.

Before running medExtractR_tapering, we first pre-processed the notes by censoring any datetime expressions. The Duration entity can include date expressions, however it was common for the SD notes to have deidentified datetime expressions unrelated to dosing. Instead, these expressions typically reflected when the note was created, the time of the appointment, or when a prescription was faxed to the pharmacy. We also removed any notes that used an XML format, due to the structure of these notes being vastly different from the typical free-text clinical notes. XML, or "extensive markup language," is a slightly more structured data format that includes tags to describe pieces of text within the note. The presence of such tags especially interfered with rule-based entities. For example, a dose amount of 3 tablets may appear as "<DOSE_AMOUNT>3</DOSE_AMOUNT><DOSE_UNIT>tablets</DOSE_UNIT>". The medExtractR system would typically consider a number followed by the word "tablets" to be a dose amount, but here the tag labels block these two expressions. Two XML-based notes were removed, resulting in 160 notes used for development.

$Details \ of \ {\tt medExtractR_tapering} \ functionality$

The tapering extension of the medExtractR function is capable of extracting more entities associated with tapering schedules, and is thus more flexible than the basic version of medExtractR. The arguments between the basic and extended versions of medExtractR are the same with one major exception: medExtractR_tapering does *not* have an argument for window_length. This is because the length of the window in which all relevant entities are contained varies greatly depending on the type of dosing schedule (e.g., taper I, taper II, or alternating). Unlike the basic medExtractR function, which uses a fixed window length, medExtractR_tapering dynamically generates a search window. This is done by first allowing a very generous search window, and then truncating based on two criteria: (1) the presence of competing drug names or terms; and (2) the distance between consecutive entities. The user can modify this search window process by adding or removing terms to the drug_list argument, for example including additional categories of competing terms to use for truncation (e.g., symptoms, procedure, or laboratory names).

```
note <- paste(scan(filename, '', sep = '\n', quiet = TRUE), collapse = '\n')
medExtractR_tapering(note, drug_names, unit, max_dist, ...)</pre>
```

The remainder of this section outlines how medExtractR_tapering processes a note, from free-text input to a structured entity-level output. We'll use the following excerpt as our example input to help illustrate how the output changes at each step.

```
Chief complaint/Reason for Visit: 4mo follow up
History of Present Illness: No muscle pain since prior visit. Does report increased fatigue.
Also reports R hand tremor intermittently.
Medications:
- Lialda 1.2 gram tablet, delayed release 4 tablets by mouth daily
- prednisone 5mg 2 tablets by mouth daily
- omeprazole 20 mg one tablet by mouth daily
Allergies:
- Penicillins (severe hives)
Past Medical and Surgical History: I have reviewed the problem list and there is no change
since last visit.
Social History:
Exercise - no change since last visit
Tobacco - no smoking
Ethanol - 1 drink per week
Employment - no change since last visit
Impression & Plan:
Doing very well today w/o symptoms and good muscle strength on exam.
1. Check CBC, CMP, CK today, and will have pt check CBC locally in 3mo
2. Taper prednisone: 10mg daily for 7 days then 5mg daily for 7 days then decrease by 1mg
every 7 days until done. Patient is on track with schedule.
3. Continue azathioprine at 200mg daily 4. Can continue to hold alendronate Follow up in
6 months.
```

Step 1: Initially, the search window is defined from the end of the previous drug mention (or the start of the note) up until the start of the next drug mention (or the end of the note). From there, medExtractR_tapering relies heavily upon expressions within the drug_list argument to further shorten the search window, truncating at the closest match on either side of the drug name of interest. The default drug_list is based on cleaned and formatted extractOns from RxNorm³ just like the basic version of medExtractR. This search window is what medExtractR_tapering provides to the extract_entities_tapering function for each drug mention.

Example: In our example note, there are two mentions of prednisone. For mention #1, the drug names "Lialda" (before) and "omeprazole" (after) serve as the boundaries of the search window. For mention #2, "Ethanol" (before) and "azathioprine" (after) are the boundaries. The search window for each mention would be:

```
MENTION 1:
1.2 gram tablet,delayed release 4 tablets by mouth daily
- prednisone 5mg 2 tablets by mouth daily
-
```

```
MENTION 2:
- 1 drink per week
```

```
Employment - no change since last visit
Impression & Plan:
Doing very well today w/o symptoms and good muscle strength on exam.
1. Check CBC, CMP, CK today, and will have pt check CBC locally in 3mo
2. Taper prednisone: 10mg daily for 7 days then 5mg daily for 7 days then decrease by
1mg every 7 days until done. Patient is on track with schedule.
3. Continue
```

Note that these are assuming drug_list incorporates only drug names, which is the default. If the user chose to augment this list with symptoms, procedures, or laboratory names, the starting point window for mention #2 could be shortened to just after "CBC" (complete blood count).

Step 2: The extract_entities_tapering function extracts all entities found within the initial search window. Strength, dose amount, dose strength, dispense amount, and refill are rule-based entities; all others are primarily dictionary-based. In the basic version of medExtractR, if a strength-like expression (e.g., "10 mg") appears in a search window with no dose amount, we would classify that as dose strength. However, in tapering schedules, it is common to have a mix of information within the same phrase, e.g., "prednisone 10mg tablet 20mg (2 tabs) daily for 2 weeks then 10mg (1 tab) daily for 2 weeks". For this reason, medExtractR relies more on the context of each strength expression to determine whether it is a strength or a dose strength. For example, if the strength expression is followed by the word "tablet" (or capsule, pill, etc.), we consider it to be "Strength" (i.e., the amount of drug per dosage unit).

Example: Below, we see that medExtractR initially extracts all entities it identifies within the search windows above. Note that for mention #1, "1.2 gram" is not extracted as a strength because for prednisone, we set unit = "mg", and hence "gram" is not a relevant unit.

MENTION 1:

entity	expr	pos
DoseAmt	4	250:251
Route	by mouth	252:260
Frequency	daily	261:266
DrugName	prednisone	269:279
${\tt Strength}$	5mg	280:283
DoseAmt	2	284:285
Route	by mouth	294:302
Frequency	daily	303:308

MENTION 2:

entity	expr	pos
Duration	per week	603:611
DoseSchedule	Taper	818:823
DrugName	prednisone	824:834
DoseStrength	10mg	836:840
Frequency	daily	841:846
Preposition	for	847:850
Duration	7 days	851:857
Transition	then	858:862
DoseStrength	5mg	863:866
Frequency	daily	867:872
Preposition	for	873:876
Duration	7 days	877:883
Transition	then	884:888
DoseChange	decrease	889:897
Preposition	by	898:900
DoseStrength	1mg	901:904

Duration	every 7 days	905:917
Preposition	until	918:923
DoseSchedule	done	924:928
Preposition	on	941:943
Preposition	with	950:954
TimeKeyword	Continue	970:978

Step 3: After extracting all entities but before returning results, extract_entities_tapering attempts to remove entities that are not likely to be associated with the drug name of interest. This is done by considering the gap, in number of characters, between consecutive entities both before and after the drug mention (the transition, preposition, and time keyword entities are excluded from this procedure due to the high potential for false positives). If this gap exceeds 50 characters, we remove all extracted entities at and further from the drug mention. The value of 50 characters was selected based on gold standard annotations on a training set of notes. Finally, we remove any prepositions or transitions from the very start or very end of the extractions, as these are primarily linkage entities and would require information on either side.

Example: There are no changes to mention #1 for this step. For mention #2, the first duration extraction of "per week" (603:611) has a gap of 207 characters until the next extraction of "Taper" (818:823). Since this exceeds the gap size of 50 characters, "per week" is removed as an unrelated entity.

MENTION 1:

mentren 1.			
entity	expr		pos
DrugName p	prednisone	269:	279
${\tt Strength}$	5mg	280:	283
DoseAmt	2	284:	285
Route	by mouth	294:	:302
Frequency	daily	303:	308
MENTION 2:			
entity	7 6	əxpr	pos
DoseSchedule	•	-	818:823
DrugName		-	824:834
DoseStrength	-	10mg	
Frequency		-	841:846
Preposition		for	847:850
Duration			851:857
Transition		-	858:862
DoseStrength		5mg	
Frequency		aily	
Preposition		for	873:876
Duration		days	
Transition		then	
DoseChange			889:897
Preposition		by	
DoseStrength		1mg	901:904
Duration		days	905:917
Preposition		ntil	918:923
DoseSchedule		done	
Preposition		on	941:943
Preposition		with	
TimeKeyword		inue	970:978
5			

Step 4: With the results returned from extract_entities_tapering, medExtractR_tapering performs some additional processing to reduce false positives. First, we look for the first occurrence of punctuation before the drug name (e.g., a period or line break), and remove all entities before that punctuation. For

example, in the phrase "... Patient was previously taking omeprazole 20mg per day. Currently on prednisone $10mg \ daily...$ ", the information "20mg" and "per day" would initially be extracted, since the window wouldn't truncate until the end of the competing drug name "omeprazole." However, since there is a period between the two sentences, medExtractR_tapering would assume "20mg" and "per day" were not related to prednisone, and thus remove them from the results. The one exception is if the adjacent entity is a preposition, which indicates it may be linking the drug mention of interest to other dosing information (e.g., "20mg of nprednisone", where "\n" is a line break). If the search window was truncated due to another drug name, we check to see if any of the entities we extracted are immediately adjacent (within 2 characters) to the competing drug name. If so, we continue to remove immediately adjacent entities until a gap of more than two characters occur (ignoring any mentions of "tablet" next to dose amount or strength), at which point we no longer attribute those extractions to the competing drug name.

Example: For mention #1 in our example, when we look at excerpt of the note between prednisone and the closest preceding entity, we see "daily\n- prednisone", where "\n" is a line break. Since there is punctuation between these two entities (in this case, either \n or - would be sufficient even without the other), we remove the extraction "daily" as well as all other extractions before it.

For mention #2, the search window was shortened by the presence of the drug name "azathioprine", and medExtractR stores the position of this competing drug name (979:991). Since "Continue" was extracted immediately before the competing drug name (970:978), we remove it from our results. No other entities are removed since there's a gap between "Continue" and the next preceding entity ("with" at 950:954).

MENTION 1:

MENIION I:			
entity	expr		pos
DrugName p	rednisone	269	:279
Strength	5mg	280	:283
DoseAmt	2	284	:285
Route	by mouth	294	:302
Frequency	daily	303	:308
MENTION 2:			
entity		ovnr	nog
DoseSchedule		expr	pos 818:823
DoseSchedule	predni	-	
DoseStrength	-		836:840
Frequency		<u> </u>	841:846
Preposition	u	•	847:850
Duration	7		851:857
Transition		•	858:862
DoseStrength	.a.	-	863:866
Frequency	a	for	867:872 873:876
Preposition	7		
Duration		-	877:883
Transition			884:888
DoseChange	decr		889:897
Preposition		by	
DoseStrength	-	1mg	901:904
	every 7 o		905:917
Preposition		ntil	918:923
DoseSchedule	(done	
Preposition		on	941:943
Preposition	1	with	950:954

The preposition and transition entities also have some additional rules applied, considering how common the expressions in these dictionaries are (e.g., "of", "to", "then", ";" or ","). For both of these entities, the

extraction must occur immediately adjacent to another extracted entity. Furthermore, for transition we require some sort of dose-relevant information to be extracted nearby (within 10 characters) on both sides. "Dose-relevant" entities include strength, dose amount, dose strength, frequency, intake time, duration, and dose schedule (for stopping keywords). Though less common, the same issue exists for the time keyword entity (common expressions include "was", "will", etc.). Rather than enforcing a character distance around time keyword extractions, we allow one word (of any length) to occur between time keyword and an adjacent entity.

Example: There are no further changes to mention #1. For mention #2, the prepositions "on" (941:943) and "with" (950:954) meet two separate conditions for removal; first, they are not immediately adjacent to another extracted entity and second, they occur at the very end of the group and we don't allow the last entity to be a preposition or transition. medExtractR_tapering combines any output from each drug mention, so the final output is:

entity	expr	pos
DrugName	prednisone	269:279
Strength	- 5mg	280:283
DoseAmt	2	284:285
Route	by mouth	294:302
Frequency	daily	303:308
DoseSchedule	Taper	818:823
DrugName	prednisone	824:834
DoseStrength	10mg	836:840
Frequency	daily	841:846
Preposition	for	847:850
Duration	7 days	851:857
Transition		858:862
DoseStrength	5mg	863:866
Frequency	daily	867:872
Preposition	for	873:876
Duration	7 days	877:883
Transition	then	884:888
DoseChange	decrease	889:897
Preposition	by	898:900
DoseStrength	1mg	901:904
Duration	every 7 days	905:917
Preposition	• •	918:923
DoseSchedule	done	924:928

References

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