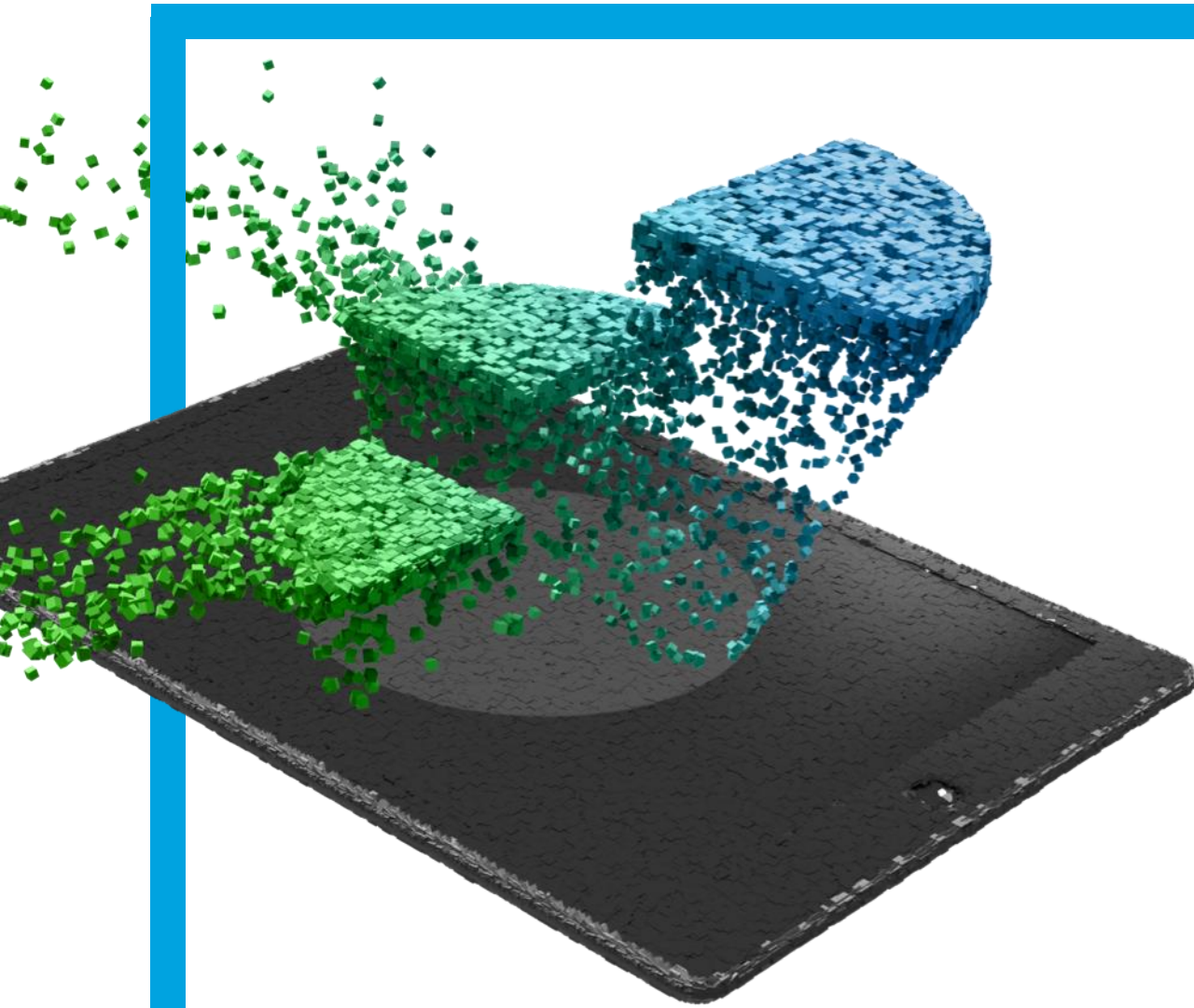




Deriving Line of Therapy:

An algorithmic approach in a real-world oncology database

Matthew Thompson, IQVIA, Leeds UK

Background: IQVIA-LTHT collaboration

Data sharing agreement: onsite team, under honorary NHS contracts, access LTHT EMR database

- Leeds Cancer Centre serves secondary care catchment area: 770,000 people
- Patients with malignant, cancer diagnosis in EMR: ~300,000
 - Patient demographics
 - Cancer diagnosis
 - Tumour staging
 - Anti-cancer therapy
 - Pathology

Retrospective, real-world study work for IQVIA clients (pharma) and LTHT clinicians

Approaching line of therapy analysis

Line of therapy (LOT) is used to describe the regimen(s) of chemotherapy a patient receives to treat their cancer

- For healthcare professionals, there is a constant desire to assess how patients respond to treatment at various LOTs
- Pharmaceutical industry develop drugs to target patients at a particular LOT
- There is real value in being able to determine:
 - › How many patients progress or are treated per line of therapy
 - › Patient endpoints per line of therapy (e.g. overall survival)
 - › Identification of meaningful cohorts for real-world studies, using line of therapy

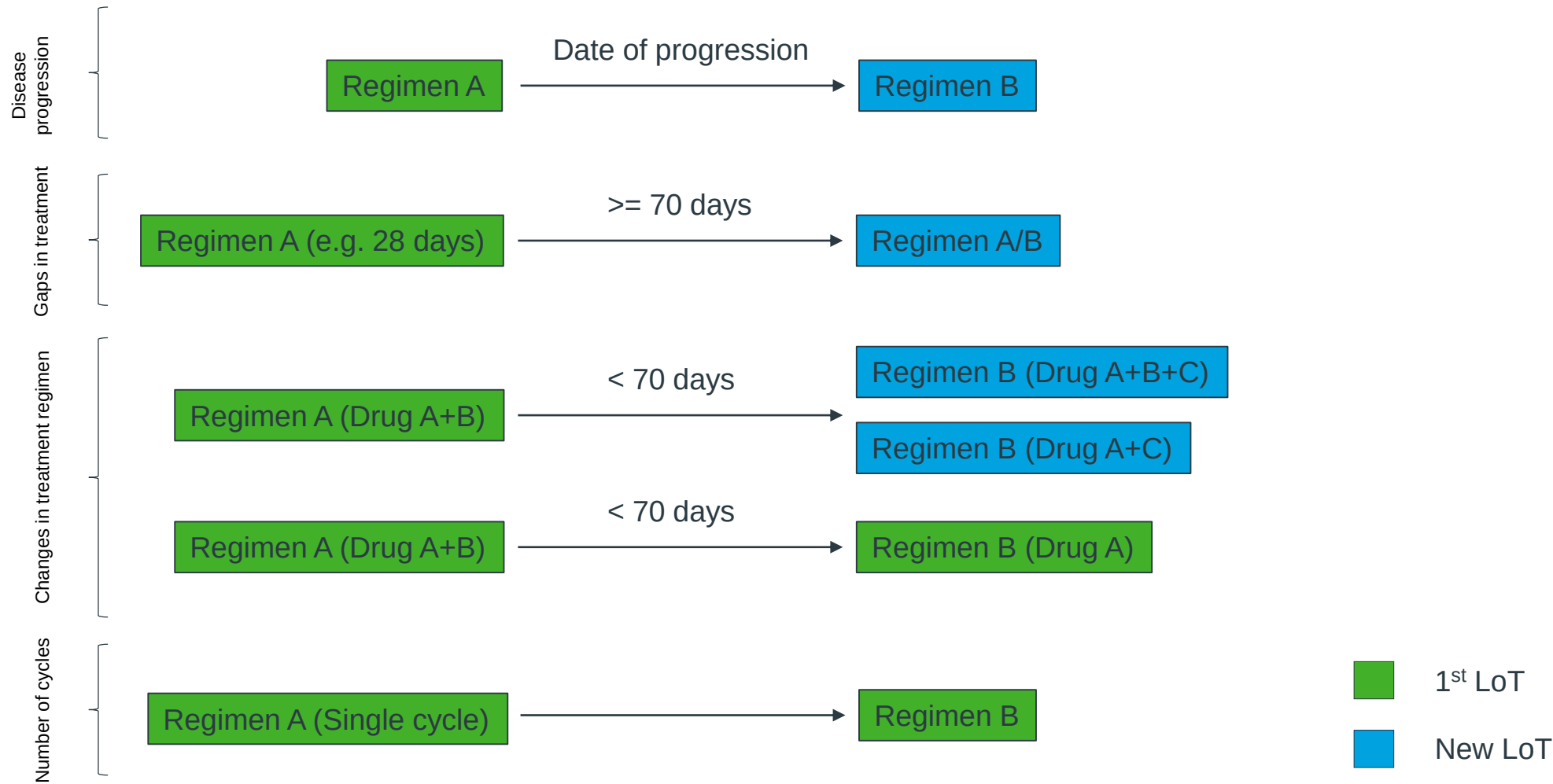
Examples of where a change in line of therapy might occur:

- **If treatment fails to control the disease**
- **If treatment is not tolerated by the patient**
- **At the point of disease relapse/progression**

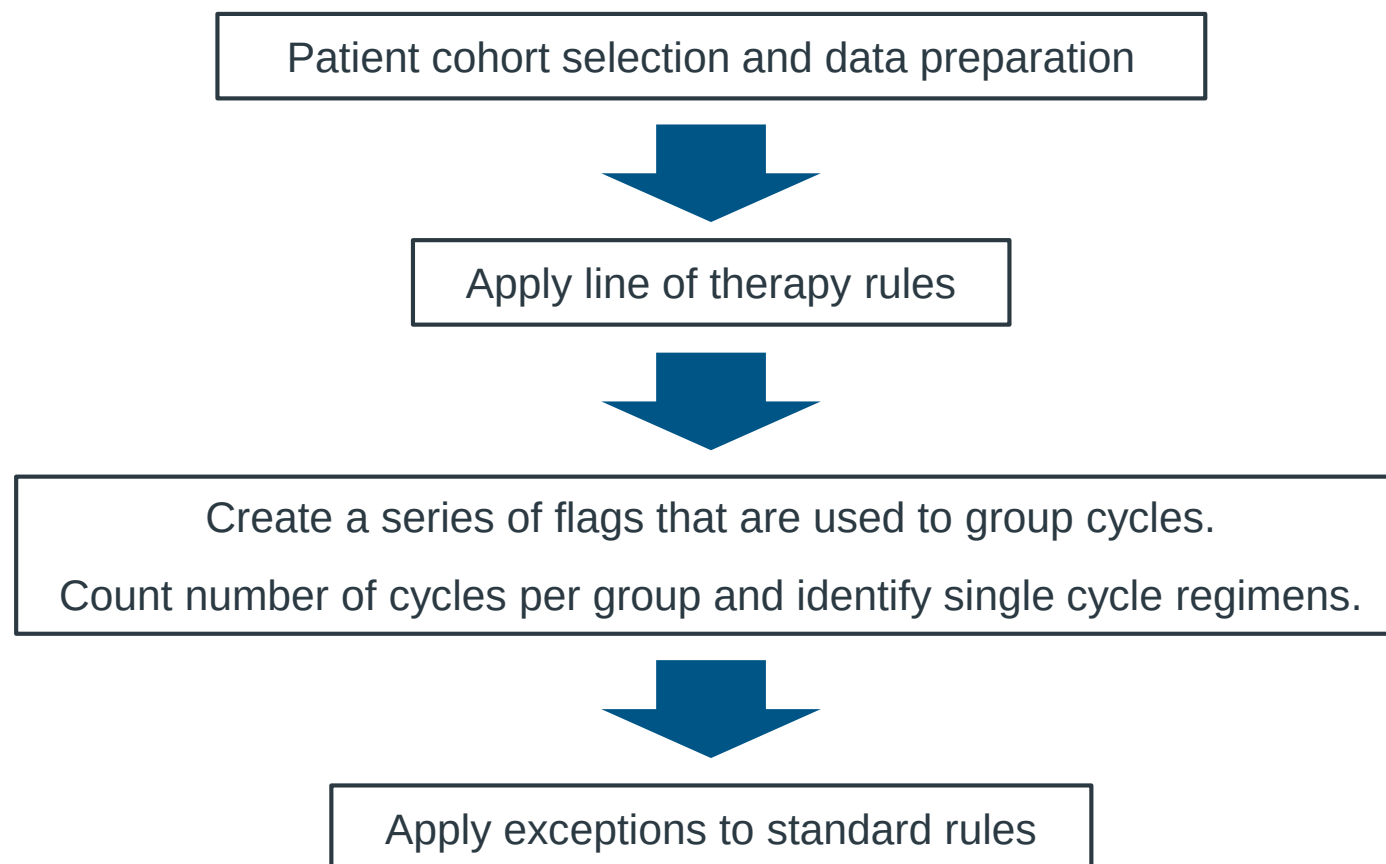
Working with a UK hospital EMR

- LOT, disease progression, treatment response/tolerance often not captured in structured or easily extractable forms
 - Must look for other indicators of change in line of therapy to derive this
- Chemotherapy data within EMR comes from ChemoCare prescribing system:
 - Regimens, cycles and drugs data are extracted and linked as part of data preparation
 - › Treatment labels: Regimen labels/descriptions + individual drug labels
 - › Cycle dates: start dates available, but no end dates
 - › Prescribed number of days for each cycle
 - › Drug administration date
 - › Number of cycles administered (derivable)
 - › Unique identifiers for linkage

We defined the following rules to identify a change in line of therapy...



A SAS algorithm has been developed...



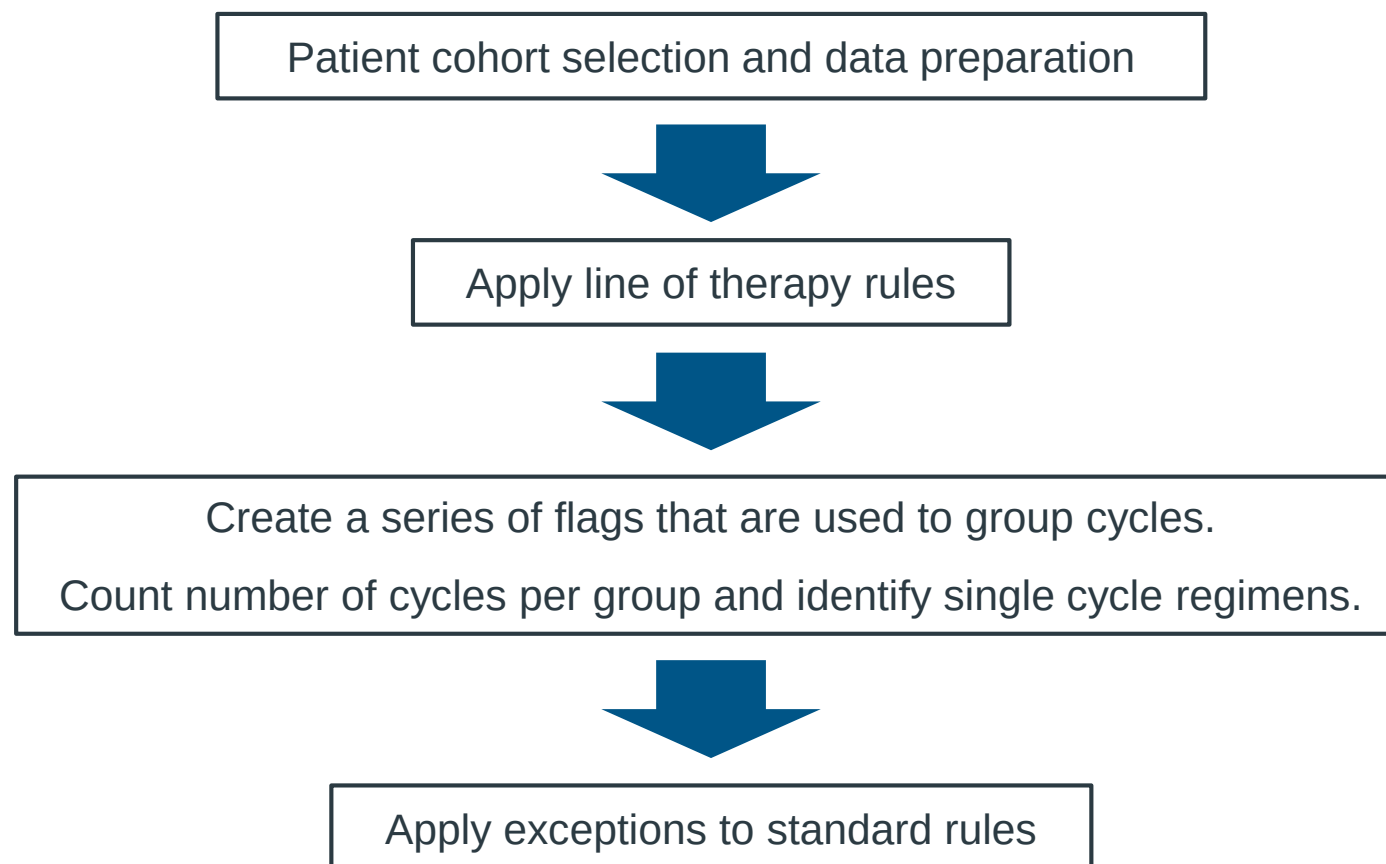
Data preparation

- Select patients with single, solid tumour cancers
- Non-standard regimen labels
 - Example: “GEM/CIS” vs. “GEM/CIS 21D” – how can we spot changes in treatment?
 - Using mapping sheets
 - › Created to align with SACT standards
 - › Removed non-chemotherapy drugs

Database Regimen Label	SACT Standardised Regimen Label	drug1	drug2	drug3
CARBO/PAC 1W L3	Carboplatin + Paclitaxel (3 weekly)	CARBOPLATIN	PACLITAXEL	
PAC L3 ALL/CARBO	Carboplatin + Paclitaxel (3 weekly)	CARBOPLATIN	PACLITAXEL	
PACLITAX/CARBO	Carboplatin + Paclitaxel (3 weekly)	CARBOPLATIN	PACLITAXEL	
CARBO/PAC 1W	Carboplatin + Paclitaxel (weekly)	CARBOPLATIN	PACLITAXEL	
CARBO/PACLITAX1W	Carboplatin + Paclitaxel (weekly)	CARBOPLATIN	PACLITAXEL	

- Regimen end dates need to be derived
 - Start date of the last cycle or last drug administration + prescribed number of days

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Using progression dates

- Compare progression dates with cycle start dates to find cycle that occurred following progression:

```
data [output];  
    set [input];  
    by patid eccstart regstart regcode;  
    array pr[*] progdt1-progdt&maxprog.; /*progression dates are included as columns*/  
    if not first.patid then do i=1 to &maxprog.;  
        /*flag cycle if progression date is between cycle start and previous cycle  
        start*/  
        if eccstart ge pr[i] and prev_strt lt pr[i] then progress=1;  
    end;  
run;
```

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Identifying gaps in treatment and switches in regimens

- The LAG function has been used to create variables containing the previous cycle's data:

```
**Identify gaps between cycles and chronological switches in regimen**;  
data cyclegap;  
  set prev_cycle;  
  by patid eccstart;  
  if not first.patid then do;  
    diff=eccstart-prev_date;  
    if regcode ne prev_reg then switch=1;  
    if diff ge 0 then gap=1;  
    if switch=1 then do; /*Check if a switch in regimen is new line of therapy*/  
      **Use SAS "sounds like" functions to determine switches between similar  
        regimens**;  
      if soundex(reglabel) = soundex(prev_rlab) then similar=1;  
      **Flag if regimen is contained in previous regimen**;  
      if index(compress(prev_rlab),compress(reglabel)) ne 0 then contain=1;  
    end;  
  end;  
run;
```

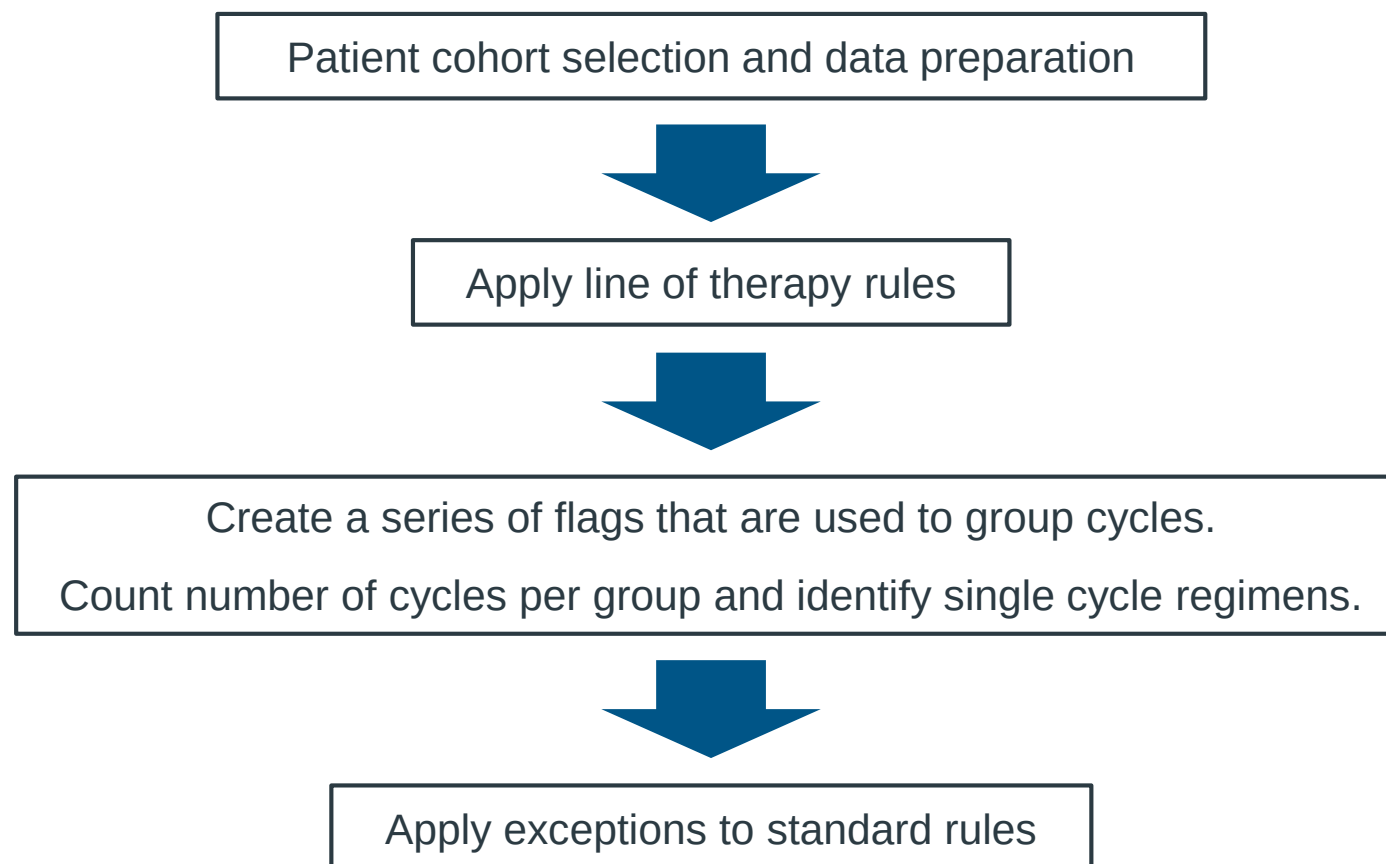
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Comparing drug combinations

```
**Compare each drug with the drugs in the previous cycle and count the number that are found in both**;
data cycledrugs2;
    set cycledrugs1;
    by patid eccstart regstart regcode reglabel;
    length pdrug1-pdrug&maxdrugs $100;
    array pd[*] pdrug1-pdrug&maxdrugs;
    array cd[*] drug1-drug&maxdrugs;
    do i=1 to &maxdrugs;
        pd[i]=lag(cd[i]); /*Use LAG function to create variables containing previous drug labels*/
    end;
    do ii=1 to &maxdrugs;
        if first.patid then pd[ii]='';
    end;
    samedrugs=0;
    do j=1 to &maxdrugs;
        do k=1 to &maxdrugs;
            if not missing(cd[j]) and (index(left(trim(pd[k])),left(trim(cd[j]))) gt 0) then samedrugs=samedrugs+1;
        end;
    end;
run;

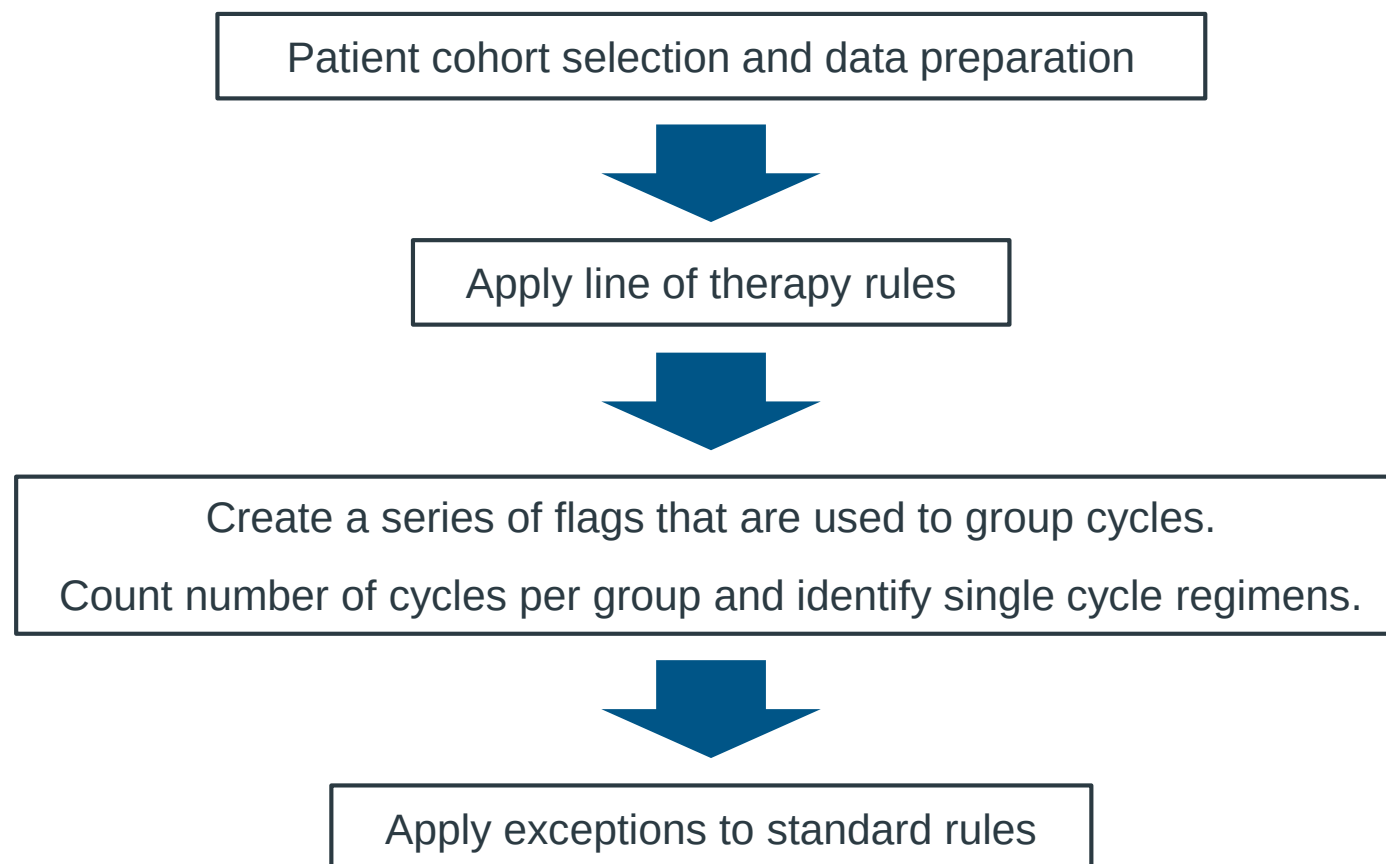
**If all drugs are in the previous cycle this means drugs are taken away and the line of therapy will not increase**;
data samedrugs;
    set cycledrugs2;
    if switch=1 and samedrugs=num_drugs and num_drugs gt 0 then contain=1;
run;
```

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patid	CycleStartDate	RegimenLabel	drug1	drug2	drug3	progress	switch	gap	similar	contain	groupno	single	NumOfCycles	new_line	LOTnum
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							1		6	1	1
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							1		6		1
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	DARBEPOETIN	PACLITAXEL						1		6		1
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	DARBEPOETIN	PACLITAXEL						1		6		1
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							1		6		1
89		CARBOPLATIN AUC 2 - 5	CARBOPLATIN				1			1	1		6		1
89		CLINICAL TRIAL TREATMENT	CARBOPLATIN	TRIAL DRUG	PACLITAXEL	1	1	1			2		15	1	2
89		CLINICAL TRIAL TREATMENT	CARBOPLATIN	TRIAL DRUG	PACLITAXEL						2		15		2
89		CLINICAL TRIAL TREATMENT	CARBOPLATIN	TRIAL DRUG	PACLITAXEL						2		15		2
89		CLINICAL TRIAL TREATMENT	CARBOPLATIN	TRIAL DRUG	PACLITAXEL						2		15		2
89		CLINICAL TRIAL TREATMENT	CARBOPLATIN	TRIAL DRUG	PACLITAXEL						2		15		2
89		CLINICAL TRIAL TREATMENT	CARBOPLATIN	TRIAL DRUG	PACLITAXEL						2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG				1			1	2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG								2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG								2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG								2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG								2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG								2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG								2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG								2		15		2
89		CLINICAL TRIAL TREATMENT	TRIAL DRUG								2		15		2
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL		1	1	1			3		18	1	3
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		3
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		3
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		3
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		3
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		3
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL				1			3		18	1	4
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		4
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		4
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		4
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		4
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		4
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL				1			3		18	1	5
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		5
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		5
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		5
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		5
89		CARBOPLATIN + PACLITAXEL (3 WEEKLY)	CARBOPLATIN	PACLITAXEL							3		18		5
89		LIPOSOMAL DOXORUBICIN 40MG/M2	LIPOSOMAL DOXORUBICIN				1	1			4		1	1	6
89		LIPOSOMAL DOXORUBICIN 40MG/M2	LIPOSOMAL DOXORUBICIN								5		3	1	7
89		LIPOSOMAL DOXORUBICIN 40MG/M2	LIPOSOMAL DOXORUBICIN								5		3		7
89		LIPOSOMAL DOXORUBICIN 40MG/M2	LIPOSOMAL DOXORUBICIN								5		3		7

A SAS algorithm has been developed...



Validation vs. clinically enhanced data

226 patients with urothelial cancer, treated with chemotherapy since 2006, with data enhanced by clinician

- PROC COMPARE of the derived LOT vs. the clinically enhanced LOT:

```
The COMPARE Procedure  
Comparison of WORK.DERIVED with WORK.ENHANCED  
(Method=EXACT)
```

Observation Summary

```
Number of Observations in Common: 1156.  
Number of Duplicate Observations found in WORK.DERIVED: 5.  
Number of Duplicate Observations found in WORK.ENHANCED: 5.  
Total Number of Observations Read from WORK.DERIVED: 1156.  
Total Number of Observations Read from WORK.ENHANCED: 1156.  
  
Number of Observations with Some Compared Variables Unequal: 7.  
Number of Observations with All Compared Variables Equal: 1149.
```

For 221 of 226 patients, the derived line of therapy matched the clinically enhanced line of therapy (97.8%)

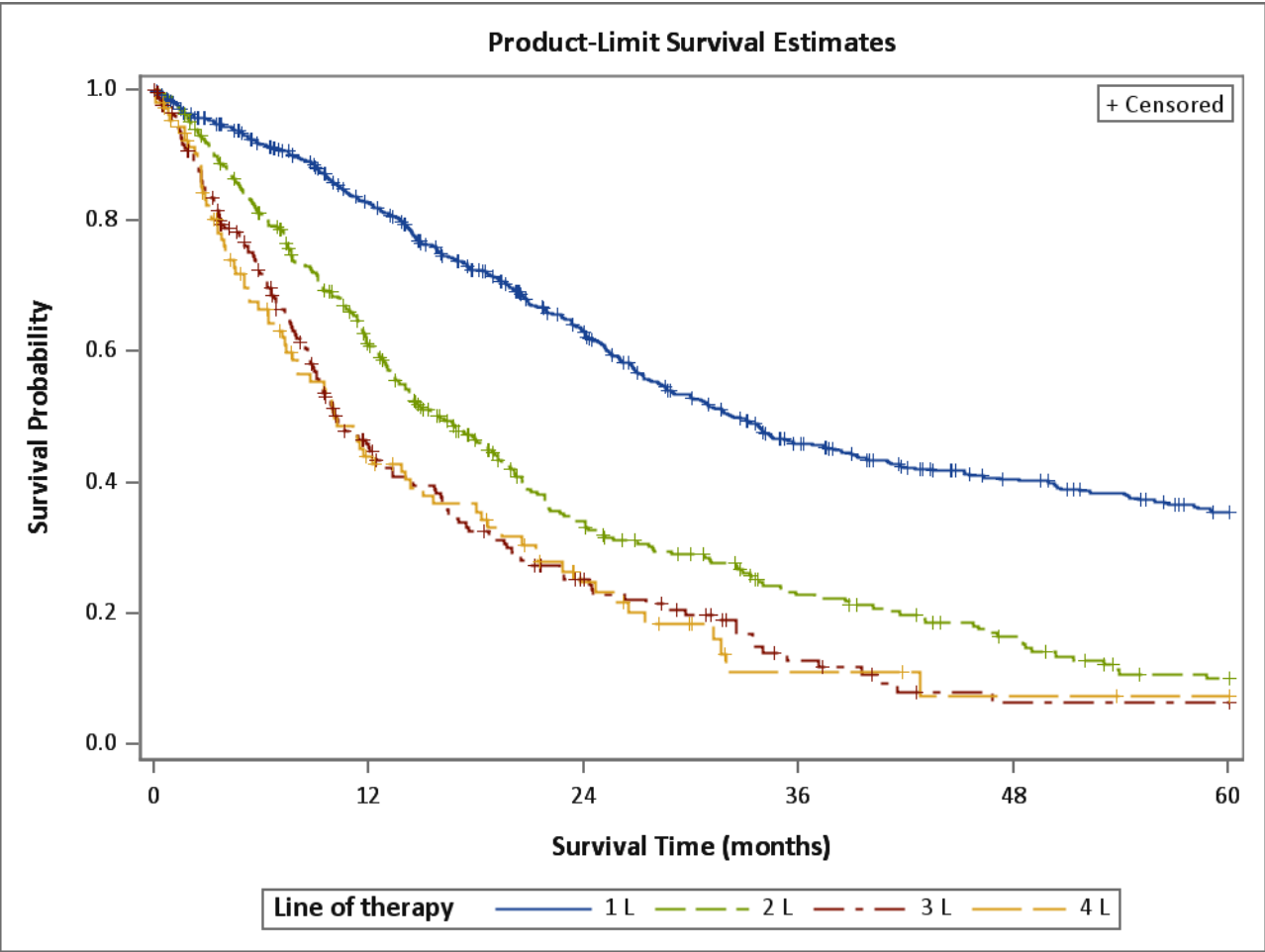
- Remaining five patients all progressed but decision was made to continue with current treatment
- Isn't detected by the derived method

Demonstrating results by line of therapy

626 patients with gynaecological cancer, treated since 2006 - LOT derived and the results reviewed by clinician

Derived line of therapy	N	%	
1 L	626	100.00	
2 L	341	54.47	
3 L	209	33.39	61.3% of 2 L
4 L	113	18.05	54.1% of 3 L
5 L+	50	7.99	44.2% of 4 L

Demonstrating results by line of therapy – overall survival



LOT	Median Survival
1 L	32.285
2 L	15.945
3 L	10.225
4 L	10.093

Conclusions

Comparing derived LOT vs. a clinically enhanced LOT for 226 urothelial cancer patients: was correct for 97.8% of patients.

2.2% (5 patients) didn't match: due to clinical decision that contradicted our rules

- For small cohorts: could be manually coded as part of exceptions step
- Illustrates the challenge in deriving LOT for 100% of cohort; there will always be exceptions to logic-based rules
 - › Complexity of treatment patterns for cancer patients

Demonstrated an ability to derive LOT and provide valuable information to healthcare and pharma industries:

- Patients treated per LOT
- Overall survival per LOT

Utilizing the method on large, retrospective cohorts saves time and resource in clinical data enhancement