R and Python code for data visualization

1. Pie chart in Python (Figure 2A)
2. Area plot in Python (Figure 2B)
3. Heatmap with numbers in R (Figure 2E)
4. Stacked bar plot in R (Figure 3A)
5. One-layer circular tree plot in R (Figure 4A)
6. Network plot with layout in circle in R (eFigure 4A)
7. Heatmap for inclusion criteria in R (Figure 5)
8. Hierarchical Pie Chart in Python (Figure 6A)
9. Heatmap for composite endpoint breakdown in R (Figure 7A)
10. Lasagna plot in R (eFigure 2A)

1. Pie chart in Python (Figure 2A)

phase

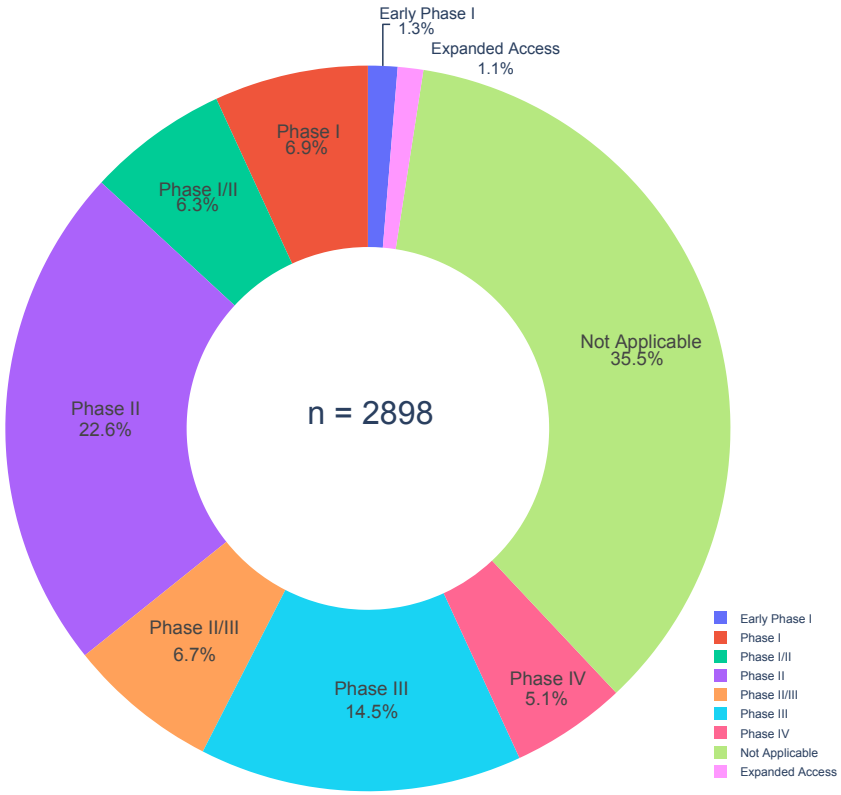
In [3]:
```
phase = pd.read_excel("~/desktop/tables_forGraph.xlsx", sheet_name = "Phase", index_col=0)
phase.loc[phase['Phase']=="Expanded Access"] == 'NA'
phase.head()
```

Out[3]:

	Phase	n	prop	ymax	ymin	labelPosition	label
1	Early Phase 1	38	0.013112	0.013112	0.000000	0.006556	Early Phase 1 1%
2	Phase 1	199	0.068668	0.081781	0.013112	0.047447	Phase 1 7%
3	Phase 1/2	182	0.062802	0.144582	0.081781	0.113182	Phase 1/2 6%
4	Phase 2	655	0.226018	0.370600	0.144582	0.257591	Phase 2 23%
5	Phase 2/3	193	0.066598	0.437198	0.370600	0.403899	Phase 2/3 7%

In [4]:
```
roman = phase['Phase'].tolist()
for p in range(len(roman)):
    roman[p] = re.sub(r'[1]+', 'I',roman[p])
    roman[p] = re.sub(r'[2]+', 'II',roman[p])
    roman[p] = re.sub(r'[3]+', 'III',roman[p])
    roman[p] = re.sub(r'[4]+', 'IV',roman[p])
phase['Phase'] = roman
```

In [5]:
```
data = go.Pie(labels=phase['Phase'], values=phase['n'] , hole=.5, textinfo = "label+percent",
              sort = False)

fig = go.Figure(data=data)
fig.update_layout(annotations=[dict(text='n = 2898',font_size=20, showarrow=False)],
                  font_family = "Arial")

fig.show()
```



2. Area plot in Python (Figure 2B)

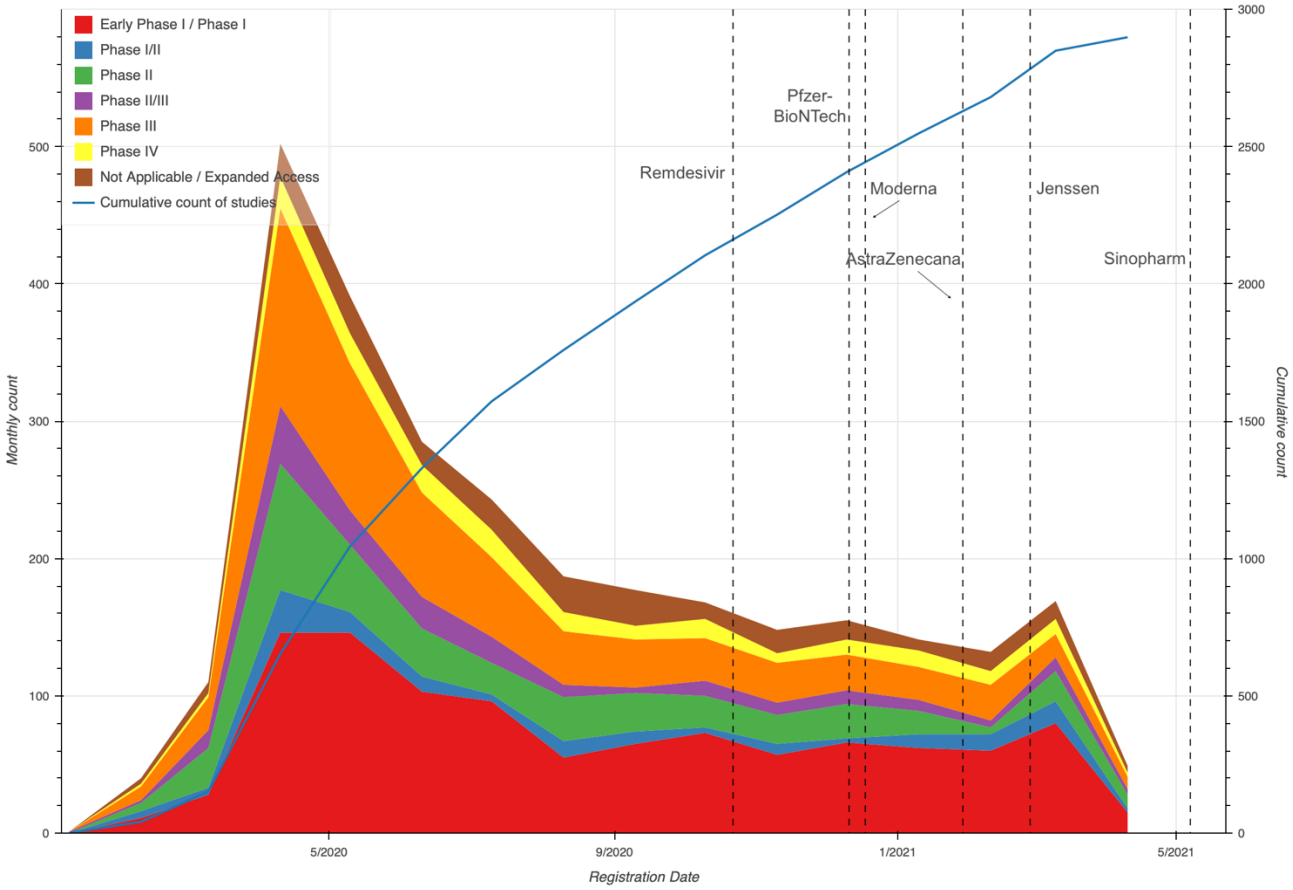
```
phase2.head()
```

	Phase	Dates	EANA	Phase 4	Phase 3	Phase 2?Phase 3	Phase 2	Phase 1?Phase 2	EP11
0		2020-01-10	0.0	0.0	0.0	1.0	0.0	0.0	0.0
1		2020-02-10	11.0	5.0	6.0	2.0	10.0	2.0	4.0
2		2020-03-10	28.0	5.0	29.0	13.0	24.0	3.0	8.0
3		2020-04-10	146.0	31.0	92.0	42.0	144.0	23.0	24.0
4		2020-05-10	146.0	15.0	51.0	25.0	107.0	22.0	27.0

```
from bokeh.io import curdoc
from bokeh.plotting import figure, output_file, show
import bokeh.palettes
from bokeh.models import Range1d, LinearAxis
from bokeh.models import Legend, LegendItem
from bokeh.models import ColumnDataSource
from bokeh.models import Label, LabelSet, Range1d, Span,BoxAnnotation
```

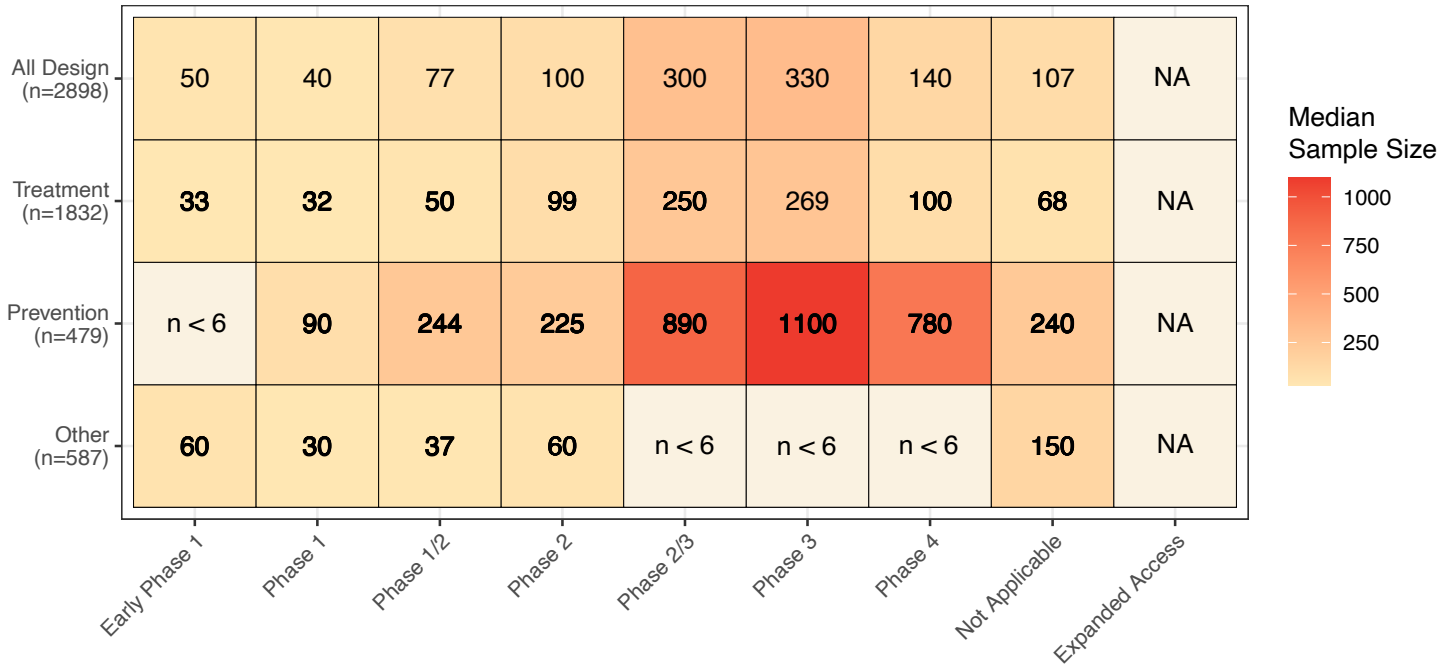
```
output_file("p.html")

p = figure(plot_width=1200, plot_height=800,x_axis_type='datetime')

cates = ['Early Phase I / Phase I', 'Phase I/II', "Phase II", "Phase II/III", "Phase III", 'Phase IV',
         'Not Applicable / Expanded Access']
colors = bokeh.palettes.brewer['Set1'][7]

## Area plot
v = p.varea_stack(['EANA', 'Phase 4','Phase 3', 'Phase 2?Phase 3', 'Phase 2',
                           'Phase 1?Phase 2', 'EP11'],
              x='Dates', color = colors ,source=phase2)

p.xaxis.axis_label = "Registration Date"
p.yaxis.axis_label = "Monthly count"

# Setting the second y axis range name and range
p.y_range = Range1d(0, 600)
p.extra_y_ranges = {"foo": Range1d(start=0, end=3000)}

# Adding the second axis to the plot.
p.add_layout(LinearAxis(y_range_name="foo",axis_label="Cumulative count"), 'right')

## line plot
v2 = p.line(y='cumulative', x = 'Dates',y_range_name="foo", line_width=2, source=phase2)
```

```
legend = Legend(items=[
    (cates[0],   [v[0]]),
    (cates[1],   [v[1]]),
    (cates[2],   [v[2]]),
    (cates[3],   [v[3]]),
    (cates[4],   [v[4]]),
    (cates[5],   [v[5]]),
    (cates[6],   [v[6]]),
    ("Cumulative count of studies",[v2]),
], location=(0, 550),background_fill_alpha=0.3)

p.add_layout(legend, 'center')

pfzer = Span(location=datetime(2020,12,11), dimension='height', line_color='black', line_width=1,
             line_dash='dashed')
moderna = Span(location=datetime(2020,12,18), dimension='height', line_color='black', line_width=1,
               line_dash='dashed')
jenssen = Span(location=datetime(2021,2,27), dimension='height', line_color='black', line_width=1,
               line_dash='dashed')
remdesivir = Span(location=datetime(2020,10,22), dimension='height', line_color='black', line_width=1,
                  line_dash='dashed')
astra = Span(location=datetime(2021,1,29), dimension='height', line_color='black', line_width=1,line_dash='dashed')
sino = Span(location=datetime(2021,5,7), dimension='height', line_color='black', line_width=1,
            line_dash='dashed')

p.renderers.extend([pfzer, moderna, jenssen, remdesivir, astra, sino])

show(p)
```


Early Phase I / Phase I
Phase I/II
Phase II
Phase II/III
Phase III
Phase IV
Not Applicable / Expanded Access
Cumulative count of studies
Remdesivir
Pfzer-
BioNTech
Moderna
AstraZenecana
Jenssen
Sinopharm
Monthly count
Cumulative count
Registration Date
0
100
200
300
400
500
0
500
1000
1500
2000
2500
3000
5/2020
9/2020
1/2021
5/2021

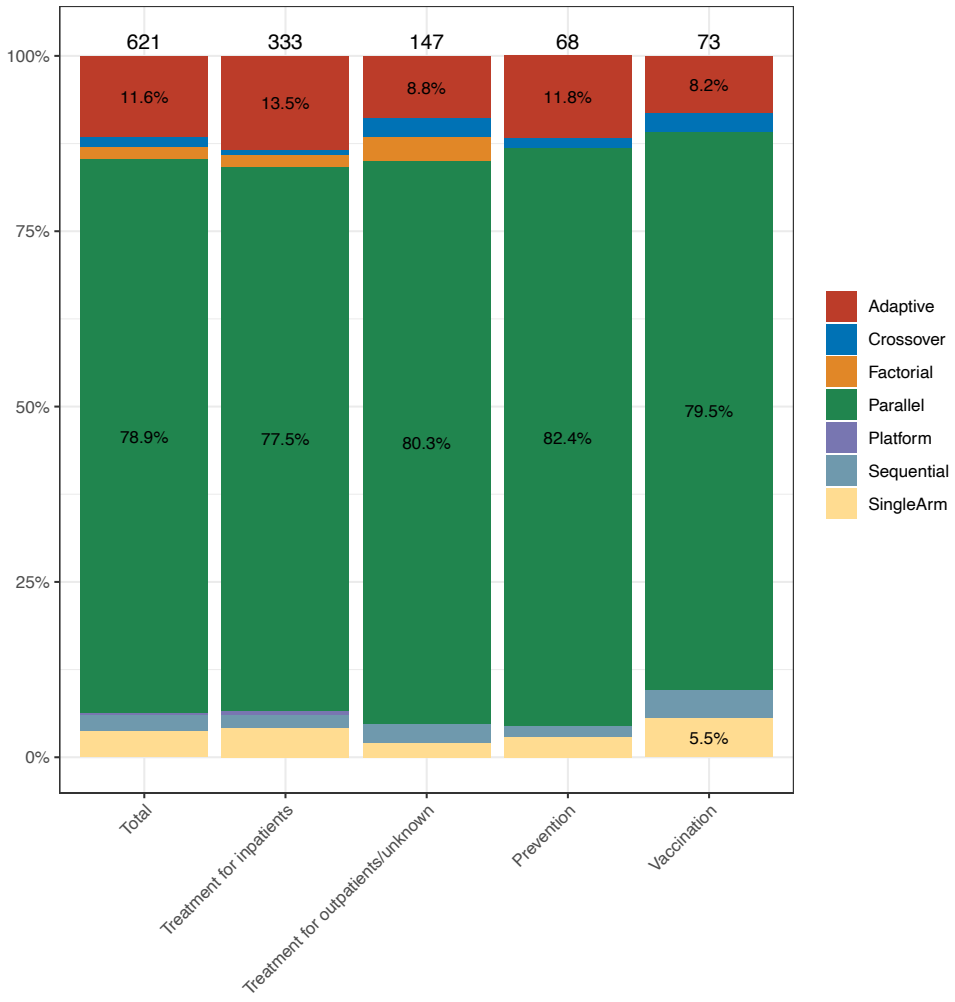
3. Heatmap with numbers in R (Figure 2E)

```
head(hpds)

## # A tibble: 6 x 4
## # Groups:   Phase [2]
##   Phase         DesignPrimaryPurpose  SampleSize     n
##   <fct>         <fct>                      <dbl> <int>
## 1 Early Phase 1 "Other\n(n=587)"              60     7
## 2 Early Phase 1 "Prevention\n(n=479)"         NA     3
## 3 Early Phase 1 "Treatment\n(n=1832)"         33    28
## 4 Phase 1       "Other\n(n=587)"              30    15
## 5 Phase 1       "Prevention\n(n=479)"         90    56
## 6 Phase 1       "Treatment\n(n=1832)"         32   128

heatmap <- ggplot(hpds, mapping = aes(x = Phase, y = DesignPrimaryPurpose, fill = SampleSize)) +
    geom_tile(color = "black") +
    geom_text(aes(label = SampleSize)) +
    scale_fill_gradient(name = "Median Sample Size",
                        low = "#ffe7b3",
                        high = "#ed3a2d",
                        na.value = "#faf2e1") +
    theme_bw() +
    theme(axis.title.y = element_blank(), axis.title.x = element_blank(), axis.text.x = element_text(angle =
45, hjust = 1) ) +
    scale_y_discrete(limits = rev(levels(as.factor(hpds$DesignPrimaryPurpose)))) +  coord_equal()
```



4. Stacked bar plot in R (Figure 3A)

```
head(SD.data)

##   Strata       Var1 Freq Tot levels Perc Perct   Total
## 1  Total   Adaptive   72 621      1 11.6 11.6% N = 621
## 2  Total  Crossover    9 621      1  1.4       N = 621
## 3  Total  Factorial   11 621      1  1.8       N = 621
## 4  Total   Parallel  491 621      1 79.1 79.1% N = 621
## 5  Total   Platform    2 621      1  0.3       N = 621
## 6  Total Sequential   14 621      1  2.3       N = 621

SD.fig <- ggplot(SD.data, aes(fill=Var1, y=Perc/100, x=reorder(Strata, +levels))) +
  geom_bar(stat="identity") +
  scale_y_continuous(labels = scales::percent) +
  geom_text(aes(label = Perct), position = position_stack(vjust = 0.5), size = 3) +
  geom_text(data = total, aes(x = Strata, y = 1, label = tot, fill = NULL), position = position_stack(vjust =
 1.02)) +
  theme_bw() +
  scale_fill_nejm()+
  theme(axis.title.x = element_blank(), axis.text.x = element_text(angle = 45, hjust=1), axis.title.y = eleme
nt_blank(), legend.title = element_blank())
SD.fig
```



5. One-layer circular tree plot in R (Figure 4A)
This was inspired by Torsten Sprenger's work (https://github.com/spren9er) and we modified his R code available at https://github.com/spren9er/tidytuesday/blob/master/tidytuesday_201946_cran_packages.r.

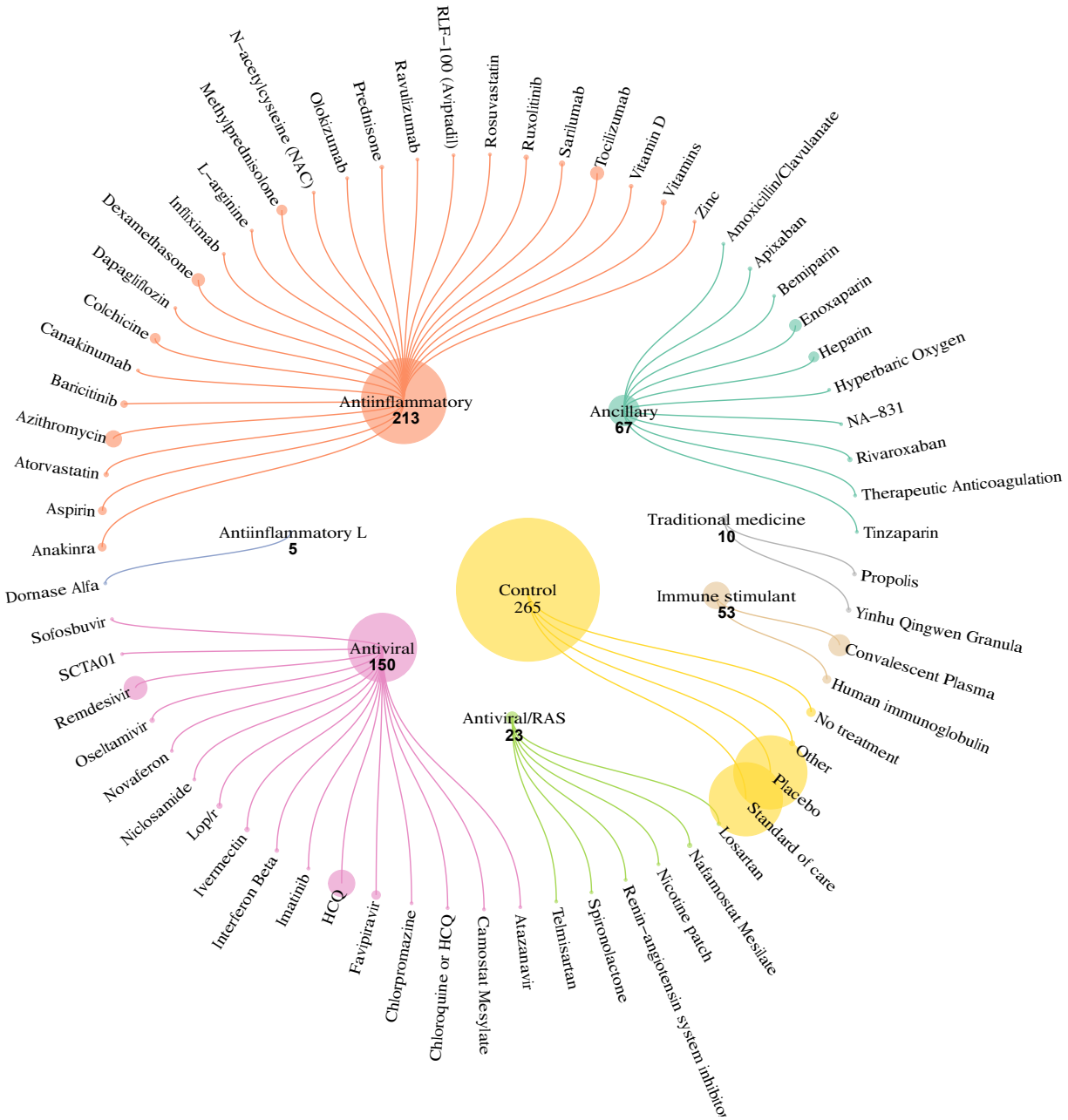
```
head(TrtLong)
```

```
## # A tibble: 6 x 4
##   Trt                    num  main Class
##   <chr>                <dbl> <dbl> <chr>
## 1 25-Hydroxyvitamin D3     1     1 Antiinflammatory
## 2 Abatacept                1     1 Antiinflammatory
## 3 ABX464                   1     1 Antiinflammatory
## 4 Acacia Senegal           1     1 Antiinflammatory
## 5 Acalabrutinib            1     1 Antiinflammatory
## 6 ACEIs                    1     1 Antiviral/RAS
```

```
# Assign colors
trtclass_colors <- c(brewer.pal(n=8,name = "Set2"), "#A6CEE3")
names(trtclass_colors)<-c(unique(TrtLong$Class),"All")

# Edges and vertices
edges1 <- TrtLong %>%
  transmute(from = Class, to = Trt, num=num, main)

edges2 <- TrtLong %>%
  dplyr::count(Class, wt = num, name = 'num') %>%
  transmute(
    from = '',
    to = Class,
    num,
    main = TRUE
  )

edges <- bind_rows(edges1, edges2)

vertices1 <- TrtLong %>%
  filter(main==1) %>%
  transmute(
    Trt = Trt, Class, num, level = 1
  )

vertices2 <- edges2 %>%
  transmute(
    Trt = to, Class = to, num, level = 2
  )

vertices3 <- tibble(
    Trt = '', Class = NA, num = 0, level = 3
)

vertices <- bind_rows(vertices1, vertices2, vertices3) %>%
  mutate(
    radius = num**(1.8), # scaling circles
    Class = factor(Class, names(trtclass_colors))
  ) %>% arrange(level, Class, Trt)

graph <- graph_from_data_frame(edges, vertices = vertices)

# Create custom layout by updating existing circle layout
layout <- create_layout(graph, layout = 'circle')

# Set outer circle
n <- nrow(TrtLong)
outer_circle <- layout %>%
```

```
  filter(level == 1) %>%
  mutate(Class = factor(Class, names(trtclass_colors))) %>%
  arrange(Class, desc(name)) %>%
  mutate(
    x = cos((row_number() - 1) / n * 2.007 * pi),
    y = sin((row_number() - 1) / n * 2.007 * pi)
  )

# Positioning circle centers manually by specifying polar coords

angles <- c(40, 120, 180, 230, 260, 310, 345, 363, 0)
radii <- c(0.5, 0.4, 0.5, 0.4, 0.5, 0.2, 0.65, 0.65, 0.5)

centers <- tibble(
  x = radii * cos(angles / 180 * pi),
  y = radii * sin(angles / 180 * pi)
)
inner_circle <- bind_cols(centers, select(filter(layout, level != 1), -x, -y))

layout[] <- bind_rows(outer_circle, inner_circle) %>% arrange(.ggraph.index)

# Plot figure
TrtClass <- ggplot(layout) +
  geom_edge_diagonal(
    aes(edge_color = node1.Class, edge_alpha = as.factor(main),),
    edge_width = 0.4, show.legend = F
  ) +
  xlim(-1.6, 1.6) + ylim(-1.4, 1.55) +
  geom_node_point(
    aes(size = radius, color = Class),
    alpha = 0.6, show.legend = FALSE
  ) +
  geom_node_text(
    aes(
      x = 1.0175 * x,
      y = 1.0175 * y,
      label = name,
      angle = -((-node_angle(x, y) + 90) %% 180) + 90,
      filter = !(name %in% TrtLong$Class)
    ),
    size = 1.8, hjust = 'outward', family = 'Arial'
  ) +
  geom_node_text(
    aes(
      x = x,
      y = y,
      label = name,
      filter = name %in% TrtLong$Class
    ),
    size = 3, hjust = 0.5, family = 'Arial', fontface = "bold"
  ) +
  geom_node_text(
    aes(
      x = x,
      y = y - 0.045,
      label = ifelse(
        num > 100,
        format(num, big.mark = ','),
        num
      ),
      filter = name %in% TrtLong$Class
    ),
    size = 3, hjust = 0.5, family = 'Arial', fontface = "bold"
  ) +
  scale_edge_color_manual(values = trtclass_colors) +
  scale_color_manual(values = trtclass_colors) +
  scale_size_area(max_size = 45) +
```

```
  scale_edge_alpha_manual(values = c(0.15, 1)) +
  coord_fixed() +
  #labs(title = 'Treatment Class (159 Treatments with 14 Classes)') +
  theme_void() +
  theme(
    text = element_text(family = 'Arial'),
    legend.position = c(0.645, 0.51),
    plot.title = element_text(face = 'bold', hjust = 0.5, size = 10))
```

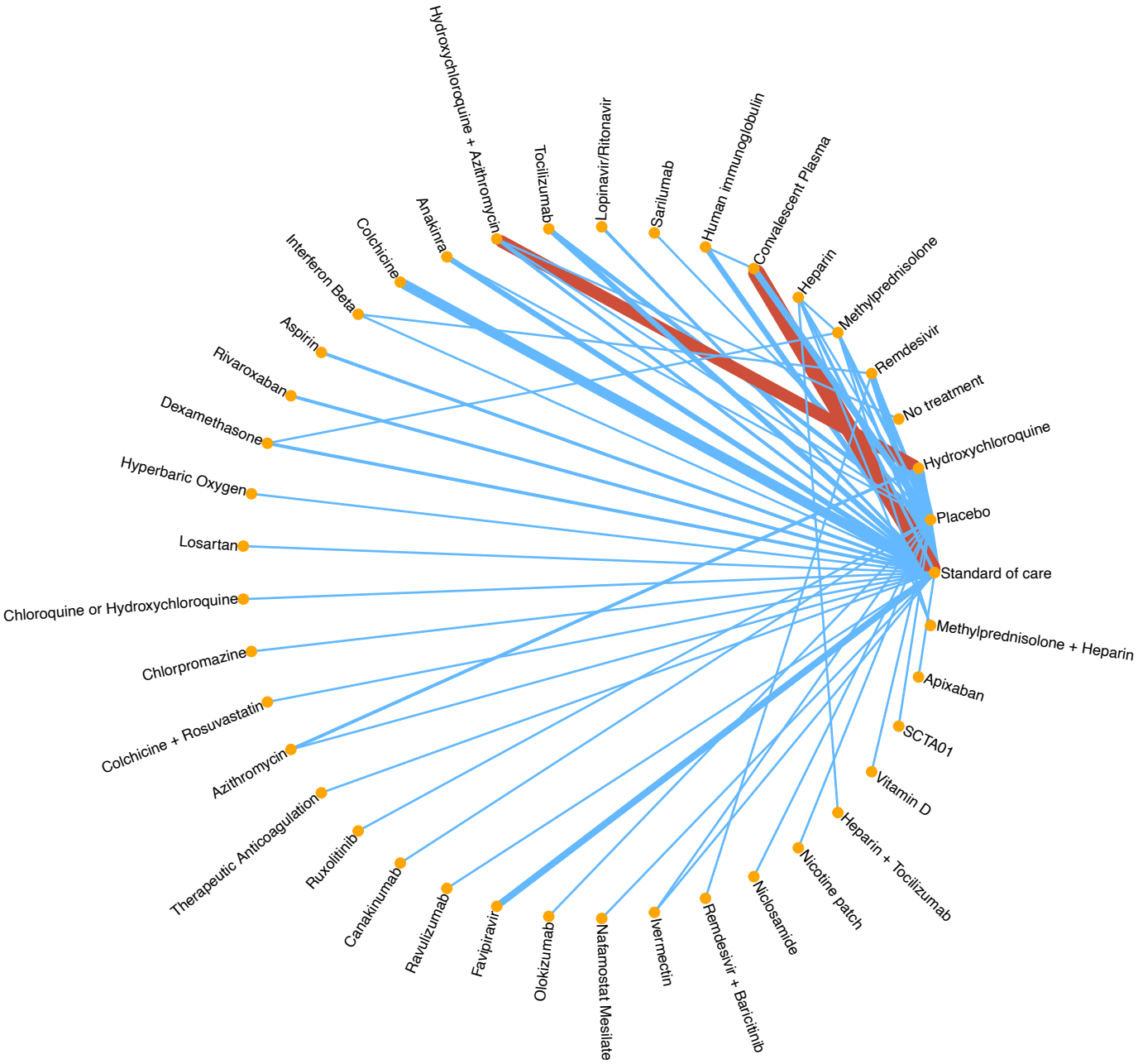


6. Network plot with layout in circle in R (eFigure 4A)

```
head(TrtLong2)
```

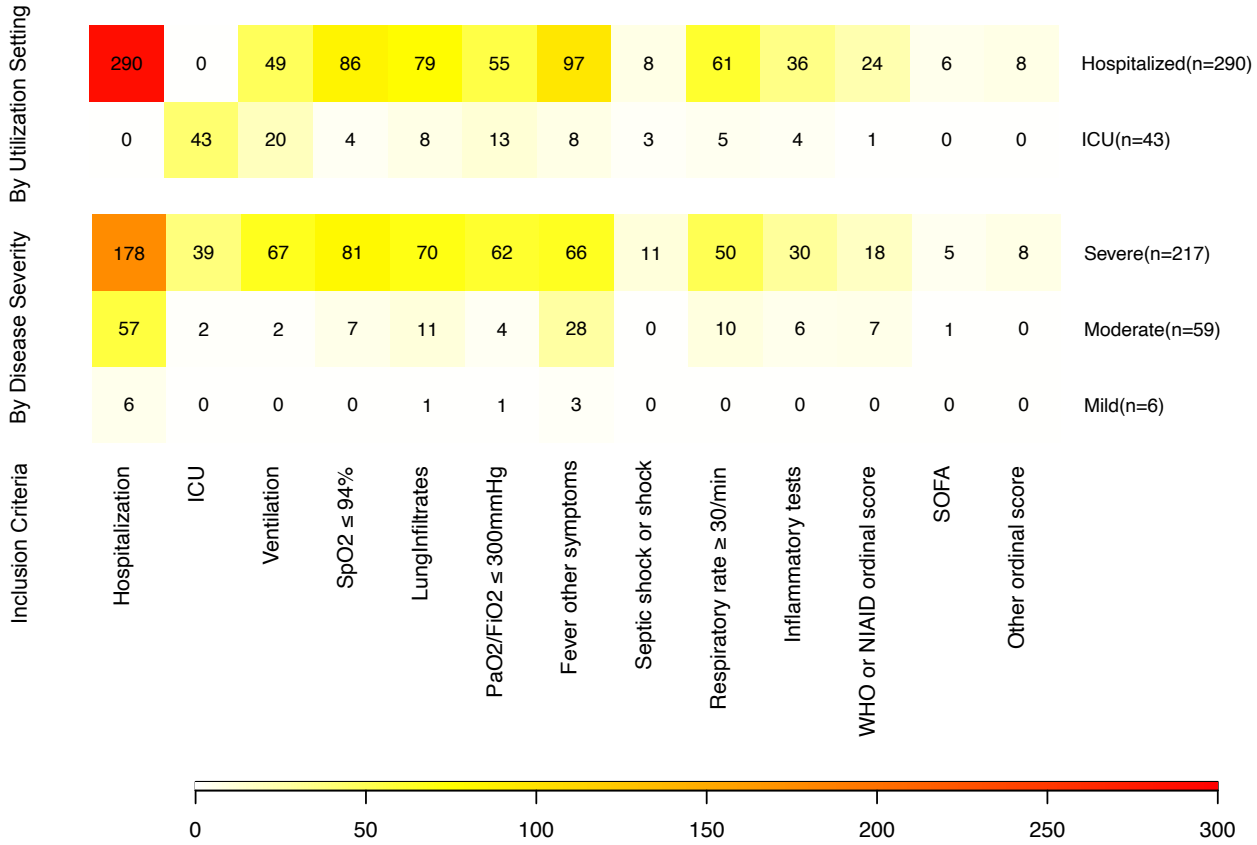
```
##               from                       to num
## 1 Standard of care      Methylprednisolone   3
## 2 Standard of care  Darunavir + Cobicistat   1
## 3          Placebo              Remdesivir   5
## 4      Oseltamivir Ritonavir + Oseltamivir   1
## 5      Oseltamivir    ASC09F + Oseltamivir   1
## 6 Standard of care    Human immunoglobulin   5
```

```
links <- TrtLong2
nodes <- data.frame(trt = unique(c(links$from, links$to)))
net <- graph_from_data_frame(d=links, vertices=nodes, directed=T)
# Adjust the node and edge size
V(net)$size <- 1
E(net)$width <- ifelse(E(net)$num>20, E(net)$num/12,
                       ifelse(E(net)$num>1, E(net)$num/2, E(net)$num/5))

# Adjust the format
V(net)$frame.color <- "orange"
V(net)$color <- "orange"
E(net)$arrow.mode <- 0
E(net)$color <- ifelse(E(net)$num>10, "tomato3",
                       ifelse(E(net)$num>1, "steelblue1", "gray"))

# Adjust the layout
l<-layout.circle(net)

# Adjust the label
x <- l[,1]*1.0175
y <- l[,2]*1.0175
angle <- -((-node_angle(x, y) + 90) %% 180) + 90

# Circle
par(mar=c(8,11,9,9))
plot(net, layout=l, vertex.label="", vertex.label.cex=0.5,
     weight.edge.lengths = edge_density(net)/4
)

# Apply the text labels with a loop with angle as srt
for (i in 12: 31) {
  text(x=x[i], y=y[i], labels=V(net)$name[i], adj=1, pos=NULL, cex=.4, col="black", srt=angle[i], xpd=T)
}
for (i in 1:11) {
  text(x=x[i], y=y[i], labels=V(net)$name[i], adj=0, pos=NULL, cex=.4, col="black", srt=angle[i], xpd=T)
}
for (i in 32: 41) {
  text(x=x[i], y=y[i], labels=V(net)$name[i], adj=0, pos=NULL, cex=.4, col="black", srt=angle[i], xpd=T)
}
```


Hydroxychloroquine + Azithromycin
Tocilizumab
Lopinavir/Ritonavir
Sarilumab
Human immunoglobulin
Convalescent Plasma
Heparin
Methylprednisolone
Remdesivir
No treatment
Hydroxychloroquine
Placebo
Standard of care
Methylprednisolone + Heparin
Apixaban
SCTA01
Vitamin D
Heparin + Tocilizumab
Nicotine patch
Niclosamide
Remdesivir + Baricitinib
Ivermectin
Nafamostat Mesilate
Olokizumab
Favipiravir
Ravulizumab
Canakinumab
Ruxolitinib
Therapeutic Anticoagulation
Azithromycin
Colchicine + Rosuvastatin
Chlorpromazine
Chloroquine or Hydroxychloroquine
Losartan
Hyperbaric Oxygen
Dexamethasone
Rivaroxaban
Aspirin
Interferon Beta
Colchicine
Anakinra

7. Heatmap for inclusion criteria in R (Figure 5)

```
head(POP.intin.u)

##                      Hospitalization ICU Ventilation SpO2<=94% LungInfiltrates
## Hospitalized(n=290)             290   0          49        86              79
## ICU(n=43)                         0  43          20         4               8
##                      PaO2/FiO2<=300mmHg Fever other symptoms Shock
## Hospitalized(n=290)                 55                   97     8
## ICU(n=43)                           13                    8     3
##                      Respiratory rate>=30/min Inflammatory tests
## Hospitalized(n=290)                       61                 36
## ICU(n=43)                                  5                  4
##                      WHO or NIAID ordinal score SOFA Other ordinal score
## Hospitalized(n=290)                         24    6                   8
## ICU(n=43)                                    1    0                   0
#Heatmap
heatmap.2(POP.intin.u,
          cellnote = POP.intin.u,  # same data set for cell labels
          cexRow=1,           #ylab size
          notecol="black",      # change font color of cell labels to black
          density.info="none",  # turns off density plot inside color legend
          trace="none",         # turns off trace lines inside the heat map
          margins =c(15,8),     # widens margins around plot
          lmat = rbind(c(0,3,0),c(2,1,0),c(0,4,0)),
          lwid = c(0.5,2,0.5),
          lhei=c(0.5,1.5,0.5),
          col=rev(heat.colors(300)),       # use on color palette defined earlier
          breaks=seq(0,300,1),
          dendrogram="none",     # only draw a row dendrogram
          Rowv=NA,
          Colv="NA")
dev.off()
```

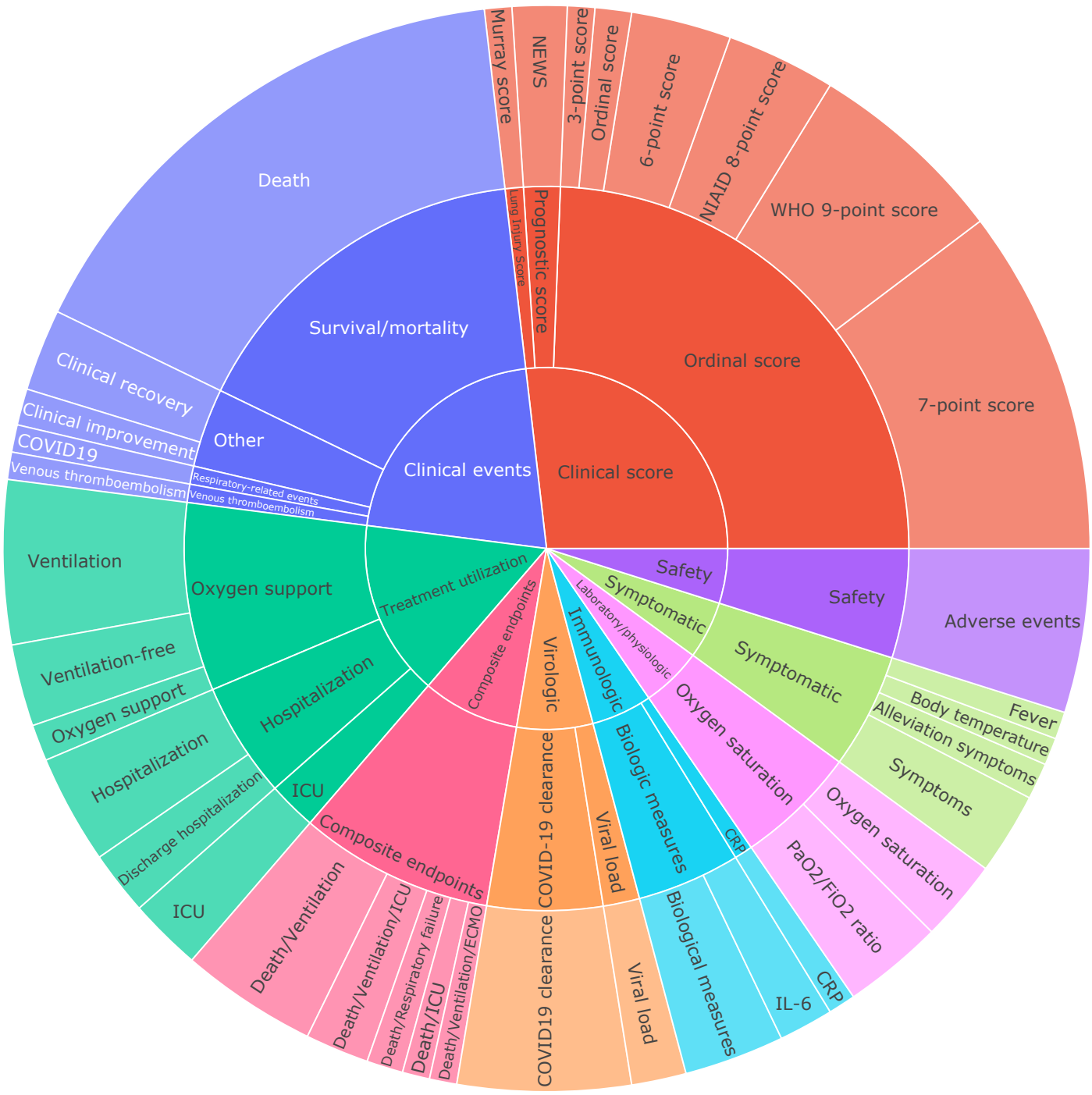


8. Hierarchical Pie Chart in Python (Figure 6A)

```
Outcomes.loc[Outcomes.Endpoint == 'None', 'Endpoint'] = None

Outcomes[['Domain','Sub-domain','Endpoint','numStudies']].head()
```

	Domain	Sub-domain	Endpoint	numStudies
0	Virologic	COVID-19 clearance	COVID19 clearance	46
1	Virologic	COVID-19 clearance	COVID19 clearance	46
2	Virologic	COVID-19 clearance	COVID19 clearance	46
3	Virologic	COVID-19 clearance	COVID19 clearance	46
4	Virologic	COVID-19 clearance	COVID19 clearance	46

```
fig = px.sunburst(Outcomes, path=['Domain','Sub-domain','Endpoint'])
fig.show()
```



9. Heatmap for composite endpoint breakdown in R (Figure 7A)

```
head(Com)
```

```
##                                             Death Ventilation
## Discharge ICU/6-point score                     0           0
## Ventilation-free/WHO 9-point score              0           1
## Discharge hospitalization/Ordinal score         0           0
## Discharge hospitalization/7-point score (n=2)   0           0
## Discharge hospitalization/Alleviation symptoms  0           0
## Discharge hospitalization/Ventilation-free      0           1
##                                             Hospitalization ICU
## Discharge ICU/6-point score                                0   1
## Ventilation-free/WHO 9-point score                         0   0
## Discharge hospitalization/Ordinal score                    0   0
## Discharge hospitalization/7-point score (n=2)              0   0
## Discharge hospitalization/Alleviation symptoms             0   0
## Discharge hospitalization/Ventilation-free                 0   0
##                                             Discharge hospitalization ECMO
## Discharge ICU/6-point score                                          0    0
## Ventilation-free/WHO 9-point score                                   0    0
## Discharge hospitalization/Ordinal score                              2    0
## Discharge hospitalization/7-point score (n=2)                        2    0
## Discharge hospitalization/Alleviation symptoms                       1    0
## Discharge hospitalization/Ventilation-free                           1    0
##                                             Ventilation-free
## Discharge ICU/6-point score                                0
## Ventilation-free/WHO 9-point score                         1
## Discharge hospitalization/Ordinal score                    0
## Discharge hospitalization/7-point score (n=2)              0
## Discharge hospitalization/Alleviation symptoms             0
## Discharge hospitalization/Ventilation-free                 1
##                                             Alleviation symptoms Intubation
## Discharge ICU/6-point score                                    0          0
## Ventilation-free/WHO 9-point score                             0          0
## Discharge hospitalization/Ordinal score                        0          0
## Discharge hospitalization/7-point score (n=2)                  0          0
## Discharge hospitalization/Alleviation symptoms                 1          0
## Discharge hospitalization/Ventilation-free                     0          0
##                                             7-point score Organ dysfunction
## Discharge ICU/6-point score                             0                 0
## Ventilation-free/WHO 9-point score                      0                 0
## Discharge hospitalization/Ordinal score                 0                 0
## Discharge hospitalization/7-point score (n=2)           2                 0
## Discharge hospitalization/Alleviation symptoms          0                 0
## Discharge hospitalization/Ventilation-free              0                 0
##                                             Arterial thromboembolism MI
## Discharge ICU/6-point score                                    0  0
## Ventilation-free/WHO 9-point score                             0  0
## Discharge hospitalization/Ordinal score                        0  0
## Discharge hospitalization/7-point score (n=2)                  0  0
## Discharge hospitalization/Alleviation symptoms                 0  0
## Discharge hospitalization/Ventilation-free                     0  0
##                                             Ordinal score Oxygen support
## Discharge ICU/6-point score                             0              0
## Ventilation-free/WHO 9-point score                      0              0
## Discharge hospitalization/Ordinal score                 2              0
## Discharge hospitalization/7-point score (n=2)           0              0
## Discharge hospitalization/Alleviation symptoms          0              0
## Discharge hospitalization/Ventilation-free              0              0
##                                             Oxygen-free Shock
## Discharge ICU/6-point score                            0     0
## Ventilation-free/WHO 9-point score                     0     0
## Discharge hospitalization/Ordinal score                0     0
## Discharge hospitalization/7-point score (n=2)          0     0
## Discharge hospitalization/Alleviation symptoms         0     0
```

```
## Discharge hospitalization/Ventilation-free              0     0
##                                            Venous thrombosis
## Discharge ICU/6-point score                                0
## Ventilation-free/WHO 9-point score                         0
## Discharge hospitalization/Ordinal score                    0
## Discharge hospitalization/7-point score (n=2)              0
## Discharge hospitalization/Alleviation symptoms             0
## Discharge hospitalization/Ventilation-free                 0
##                                            Additional treatment ARDS
## Discharge ICU/6-point score                                0    0
## Ventilation-free/WHO 9-point score                         0    0
## Discharge hospitalization/Ordinal score                    0    0
## Discharge hospitalization/7-point score (n=2)              0    0
## Discharge hospitalization/Alleviation symptoms             0    0
## Discharge hospitalization/Ventilation-free                 0    0
##                                            Arterial thrombosis
## Discharge ICU/6-point score                                0
## Ventilation-free/WHO 9-point score                         0
## Discharge hospitalization/Ordinal score                    0
## Discharge hospitalization/7-point score (n=2)              0
## Discharge hospitalization/Alleviation symptoms             0
## Discharge hospitalization/Ventilation-free                 0
##                                            Cardiac arrest
## Discharge ICU/6-point score                             0
## Ventilation-free/WHO 9-point score                      0
## Discharge hospitalization/Ordinal score                 0
## Discharge hospitalization/7-point score (n=2)           0
## Discharge hospitalization/Alleviation symptoms          0
## Discharge hospitalization/Ventilation-free              0
##                                            Cardiovascular organ support
## Discharge ICU/6-point score                                          0
## Ventilation-free/WHO 9-point score                                   0
## Discharge hospitalization/Ordinal score                              0
## Discharge hospitalization/7-point score (n=2)                        0
## Discharge hospitalization/Alleviation symptoms                       0
## Discharge hospitalization/Ventilation-free                           0
##                                            Discharge ICU
## Discharge ICU/6-point score                          1
## Ventilation-free/WHO 9-point score                   0
## Discharge hospitalization/Ordinal score              0
## Discharge hospitalization/7-point score (n=2)        0
## Discharge hospitalization/Alleviation symptoms       0
## Discharge hospitalization/Ventilation-free           0
##                                            Intravascular coagulation
## Discharge ICU/6-point score                                     0
## Ventilation-free/WHO 9-point score                              0
## Discharge hospitalization/Ordinal score                         0
## Discharge hospitalization/7-point score (n=2)                   0
## Discharge hospitalization/Alleviation symptoms                  0
## Discharge hospitalization/Ventilation-free                      0
##                                            Non-hemorrhagic stroke
## Discharge ICU/6-point score                                   0
## Ventilation-free/WHO 9-point score                            0
## Discharge hospitalization/Ordinal score                       0
## Discharge hospitalization/7-point score (n=2)                 0
## Discharge hospitalization/Alleviation symptoms                0
## Discharge hospitalization/Ventilation-free                    0
##                                            6-point score WHO 9-point score
## Discharge ICU/6-point score                          1                 0
## Ventilation-free/WHO 9-point score                   0                 1
## Discharge hospitalization/Ordinal score              0                 0
## Discharge hospitalization/7-point score (n=2)        0                 0
## Discharge hospitalization/Alleviation symptoms       0                 0
## Discharge hospitalization/Ventilation-free           0                 0
##                                            Pulmonary embolism Renal failure
## Discharge ICU/6-point score                             0             0
```

```
## Ventilation-free/WHO 9-point score                                  0            0
## Discharge hospitalization/Ordinal score                             0            0
## Discharge hospitalization/7-point score (n=2)                       0            0
## Discharge hospitalization/Alleviation symptoms                      0            0
## Discharge hospitalization/Ventilation-free                          0            0
##                                                 Respiratory failure SOFA Stroke
## Discharge ICU/6-point score                                       0    0      0
## Ventilation-free/WHO 9-point score                                0    0      0
## Discharge hospitalization/Ordinal score                           0    0      0
## Discharge hospitalization/7-point score (n=2)                     0    0      0
## Discharge hospitalization/Alleviation symptoms                    0    0      0
## Discharge hospitalization/Ventilation-free                        0    0      0
##                                                 Venous thromboembolism
## Discharge ICU/6-point score                                          0
## Ventilation-free/WHO 9-point score                                   0
## Discharge hospitalization/Ordinal score                              0
## Discharge hospitalization/7-point score (n=2)                        0
## Discharge hospitalization/Alleviation symptoms                       0
## Discharge hospitalization/Ventilation-free                           0
##                                                 Clinical improvement
## Discharge ICU/6-point score                                        0
## Ventilation-free/WHO 9-point score                                 0
## Discharge hospitalization/Ordinal score                            0
## Discharge hospitalization/7-point score (n=2)                      0
## Discharge hospitalization/Alleviation symptoms                     0
## Discharge hospitalization/Ventilation-free                         0
##                                                 Rescue medication
## Discharge ICU/6-point score                                     0
## Ventilation-free/WHO 9-point score                              0
## Discharge hospitalization/Ordinal score                         0
## Discharge hospitalization/7-point score (n=2)                   0
## Discharge hospitalization/Alleviation symptoms                  0
## Discharge hospitalization/Ventilation-free                      0

heatmap.2(Com,
          cexRow=1,           #ylab size
          cexCol=1,
          density.info="none",  # turns off density plot inside color legend
          trace="none",         # turns off trace lines inside the heat map
          margins =c(12,10),     # widens margins around plot
          lwid = c(0.2,4.5,2.8),
          lmat = rbind(c(0,3,0),c(2,1,0),c(0,4,0)),
          lhei=c(0.5,3.5,0.5),
          col=c("gray95","#FC9272","#FB6A4A", "#EF3B2C", "#CB181D", "#A50F15","#67000D"),
          breaks=c(0,0.1,1,2,3,4,7,15),
          dendrogram="none",     # only draw a row dendrogram
          Rowv=NA,
          Colv="NA")
dev.off()
```


Discharge ICU/6−point score
Ventilation−free/WHO 9−point score
Discharge hospitalization/Ordinal score
Discharge hospitalization/7−point score (n=2)
Discharge hospitalization/Alleviation symptoms
Discharge hospitalization/Ventilation−free
Hospitalization/Clinical improvement
Hospitalization/Oxygen support (n=2)
Ventilation/Oxygen support/ICU/Rescue medication
Ventilation/Oxygen support
Ventilation/ECMO/Oxygen support
Ventilation/ECMO
Ventilation/ICU (n=2)
Death/Respiratory failure (n=4)
Death/Venous thrombosis/Arterial thrombosis/Intravascular coagulation
Death/Venous thromboembolism/Arterial thromboembolism
Death/Venous thromboembolism
Death/Arterial thromboembolism/MI/Shock/Venous thrombosis/Cardiac arrest/Pulmonary embolism/Stroke
Death/Arterial thromboembolism/MI/Venous thromboembolism/Venous thrombosis/Cardiac arrest/Pulmonary embolism/Stroke
Death/Organ dysfunction (n=2)
Death/Intubation (n=2)
Death/ECMO/Venous thromboembolism/Arterial thrombosis
Death/ECMO
Death/ICU (n=3)
Death/Alleviation symptoms/Oxygen−free/Ventilation−free (n=2)
Death/Hospitalization/Ventilation/ICU
Death/Hospitalization
Death/Ventilation/Intubation/Arterial thromboembolism/MI/Non−hemorrhagic stroke/Venous thromboembolism
Death/Ventilation/ECMO/Cardiovascular organ support/Renal failure
Death/Ventilation/ICU/ARDS/Venous thrombosis/Arterial thrombosis
Death/Ventilation/ICU/Additional treatment
Death/Ventilation/SOFA
Death/Ventilation/Oxygen support
Death/Ventilation/ECMO (n=3)
Death/Ventilation/ICU (n=7)
Death/Ventilation (n=15)
Death
Ventilation
Hospitalization
ICU
Discharge hospitalization
ECMO
Ventilation−free
Alleviation symptoms
Intubation
7−point score
Organ dysfunction
Arterial thromboembolism
MI
Ordinal score
Oxygen support
Oxygen−free
Shock
Venous thrombosis
Additional treatment
ARDS
Arterial thrombosis
Cardiac arrest
Cardiovascular organ support
Discharge ICU
Intravascular coagulation
Non−hemorrhagic stroke
6−point score
WHO 9−point score
Pulmonary embolism
Renal failure
Respiratory failure
SOFA
Stroke
Venous thromboembolism
Clinical improvement
Rescue medication
0
5
10
15

10. Lasagna plot in R (eFigure 2A)

```
head(longer_actual)

## # A tibble: 6 x 5
##   NCTId       StudyType2_simple OverallStatus dates      value
##   <chr>       <chr>             <chr>         <date>     <fct>
## 1 NCT04244591 Intervention      Completed     2020-01-01 0
## 2 NCT04244591 Intervention      Completed     2020-01-02 0
## 3 NCT04244591 Intervention      Completed     2020-01-03 0
## 4 NCT04244591 Intervention      Completed     2020-01-04 0
## 5 NCT04244591 Intervention      Completed     2020-01-05 0
## 6 NCT04244591 Intervention      Completed     2020-01-06 0

## by overall status
lasagna_status = ggplot(longer_actual, mapping = aes(x = dates, y = NCTId , fill = value)) +
    geom_tile()  +  xlab("Year") +
  facet_grid(OverallStatus~., scales = "free", labeller = as_labeller(statuslabel))+
  scale_fill_manual(values = c("grey","#fc4e2a","#800026","white"),labels=c("Before registration", "Registrat
ion--start","Started","Completed")) +
  theme(axis.text.y = element_blank(), axis.ticks.y = element_blank(), axis.title.y = element_blank(),
        panel.background = element_blank(),
          plot.background = element_blank(),
        strip.text.y = element_text(angle = 0), legend.title = element_blank()) + geom_vline(aes(xintercept=a
s.Date("2022-01-09", format="%Y-%m-%d")), colour="#6495ED")
```