

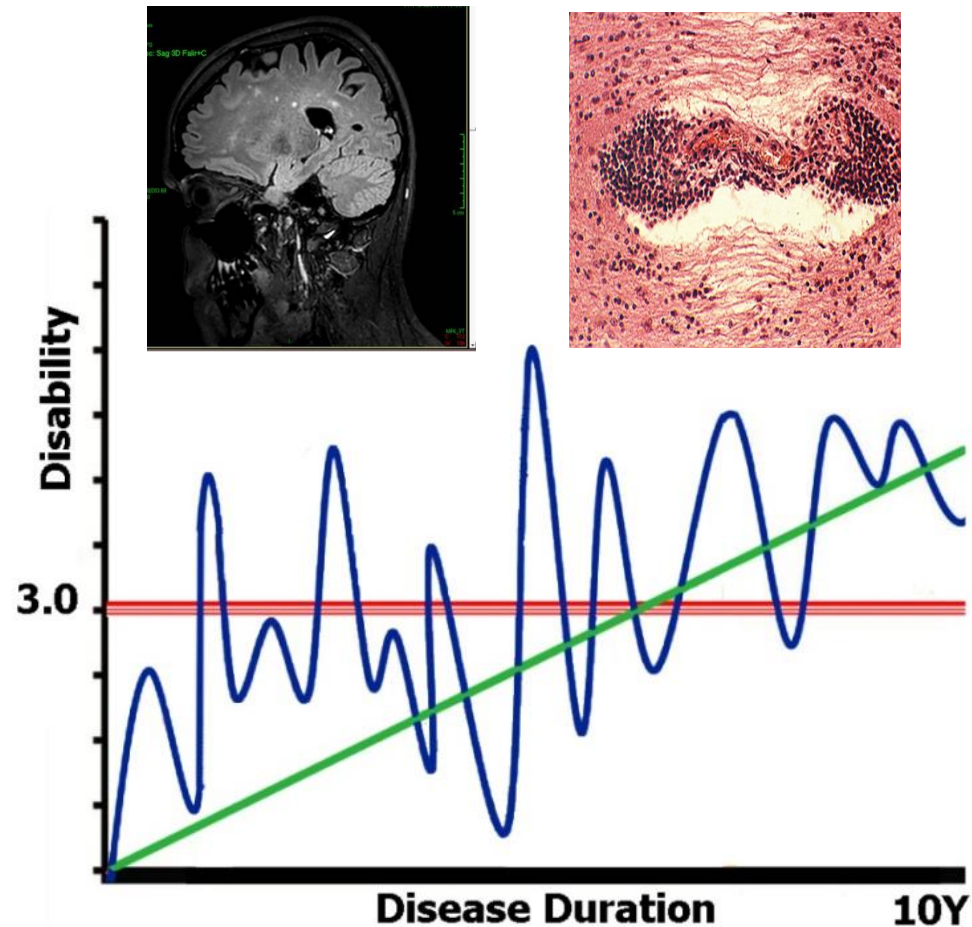


Cytokines profile in acute multiple sclerosis relapses: characterization of pattern and prediction of clinical relapse outcome

Prof Anat Achiron, Multiple Sclerosis Center
Student: Sean Zadik, 3rd year, LC program

Multiple sclerosis – A devastating disease in young adults

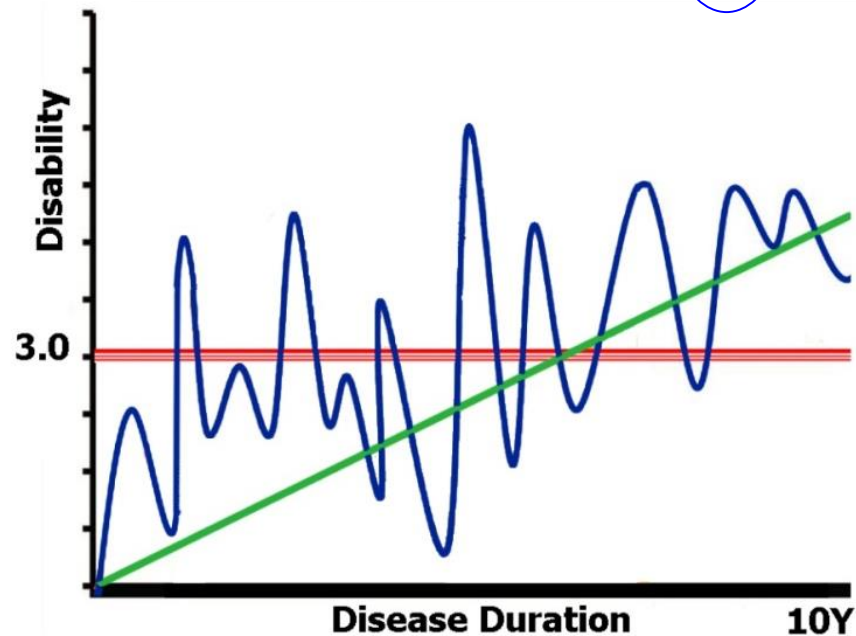
Relapsing-remitting MS (RRMS) occurs in ~85% of patients



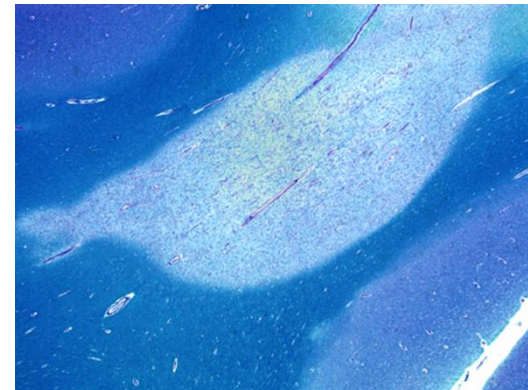
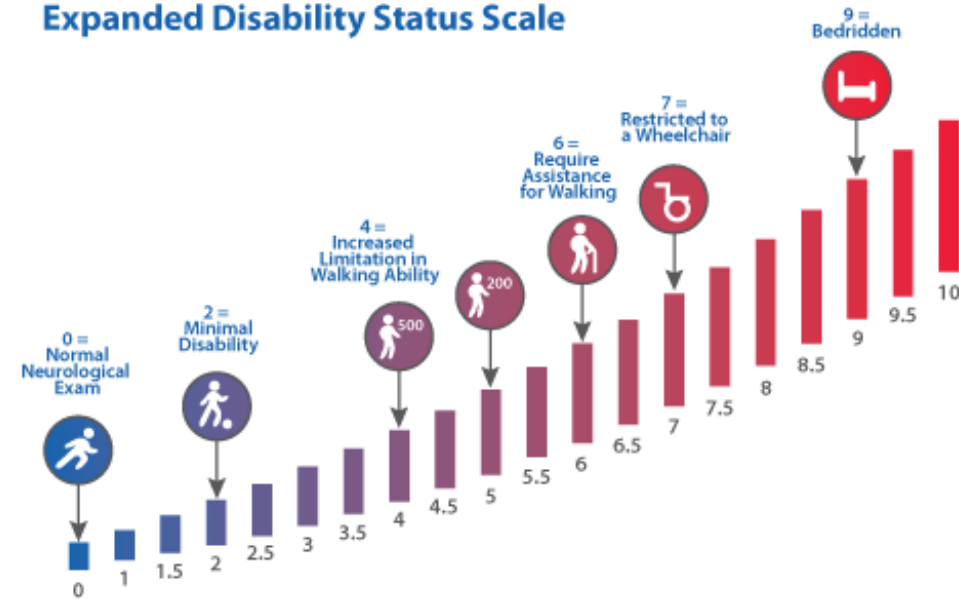
	At Onset
Motor	26.6
Sensory	25.3
Visual	21.4
Balance	14.2
Sphincters	14.2
Cognition	1.4

MS causing disability progression in young adults

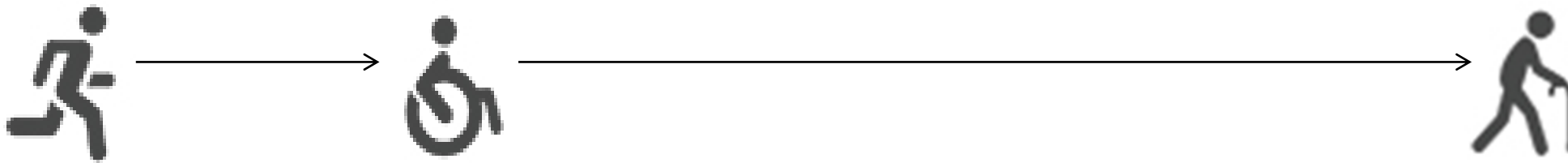
	At Onset	After 10 to 15 years
Motor	26.6	94.2
Sensory	25.3	78.2
Visual	21.4	63.9
Balance	14.2	71.6
Sphincters	14.2	71.4
Cognition	1.4	14.6



Expanded Disability Status Scale



The **Volcano** Eruption of Acute MS Relapse



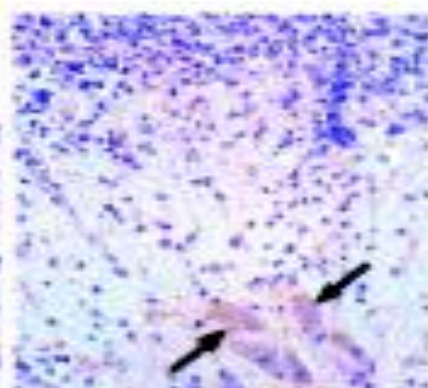
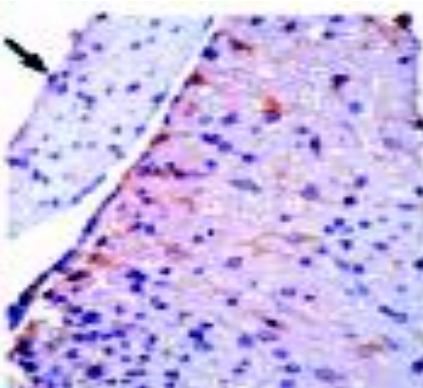
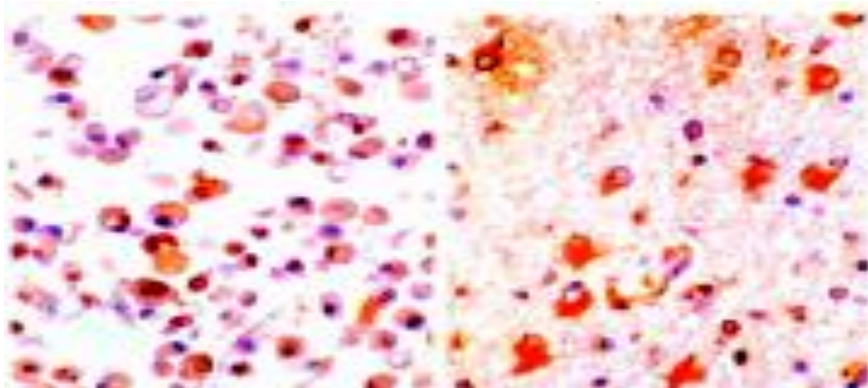
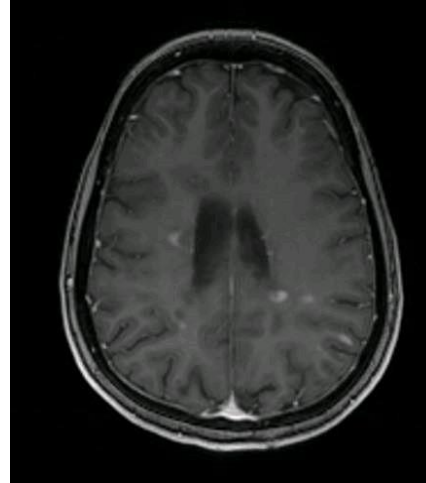
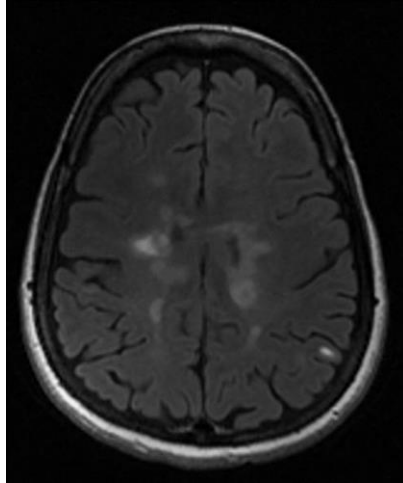
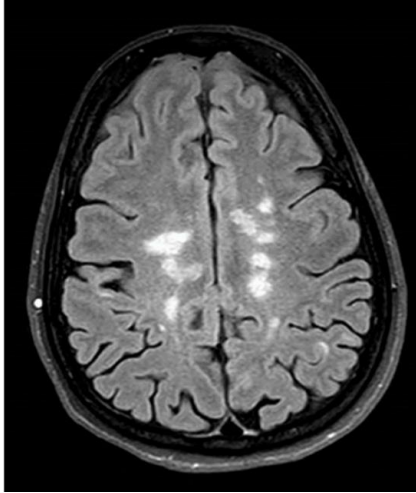
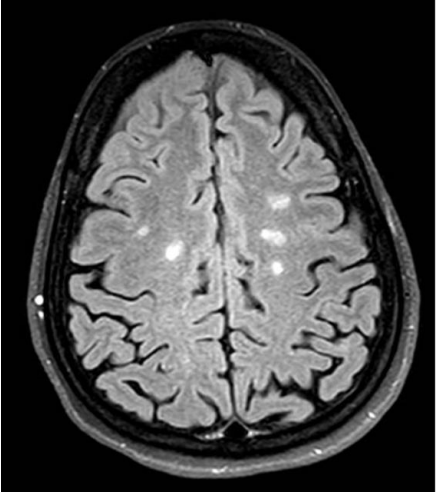
ACUTE DAMAGE



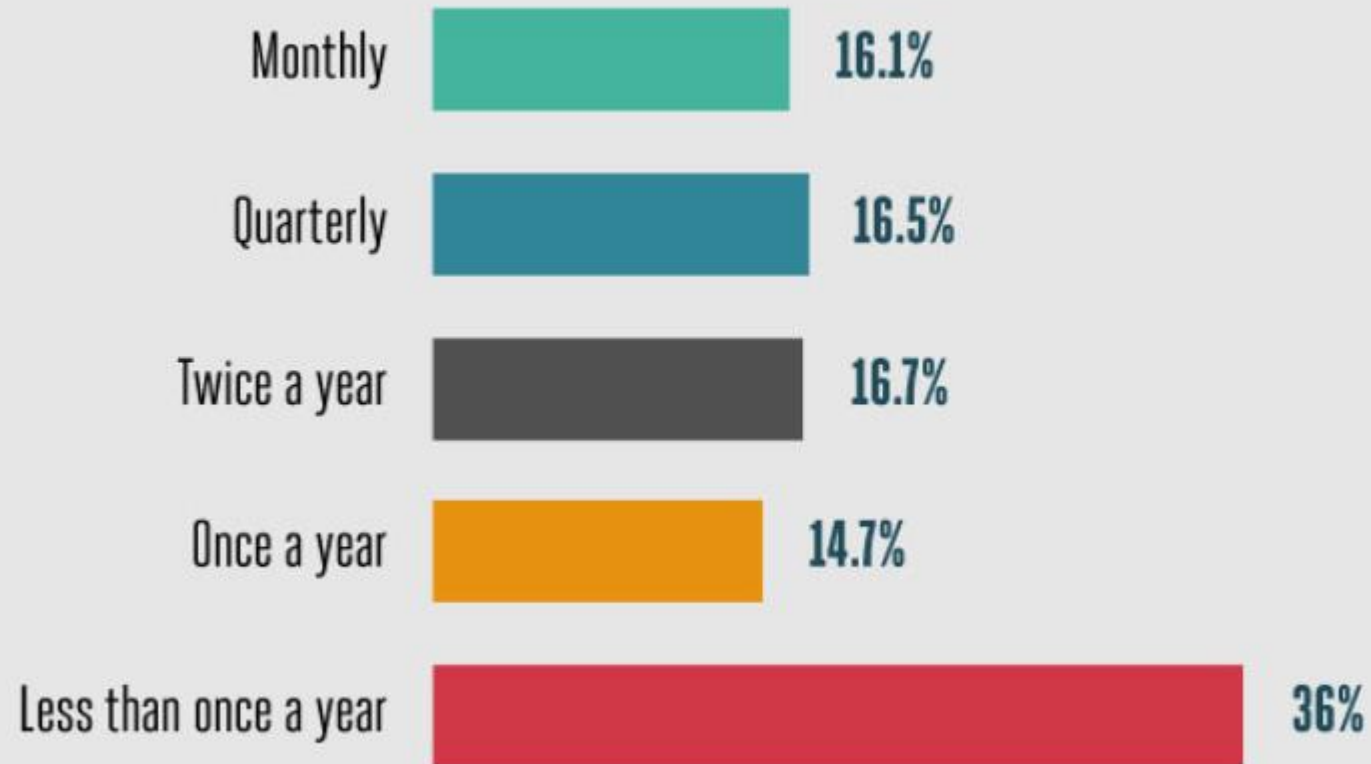
PERSISTENT DAMAGE

Approx. 200,000 relapses to be treated in US and EU per year

Acute Multiple Sclerosis Relapse: Immunological attack in the CNS



How frequently on average do you experience relapses/exacerbations?



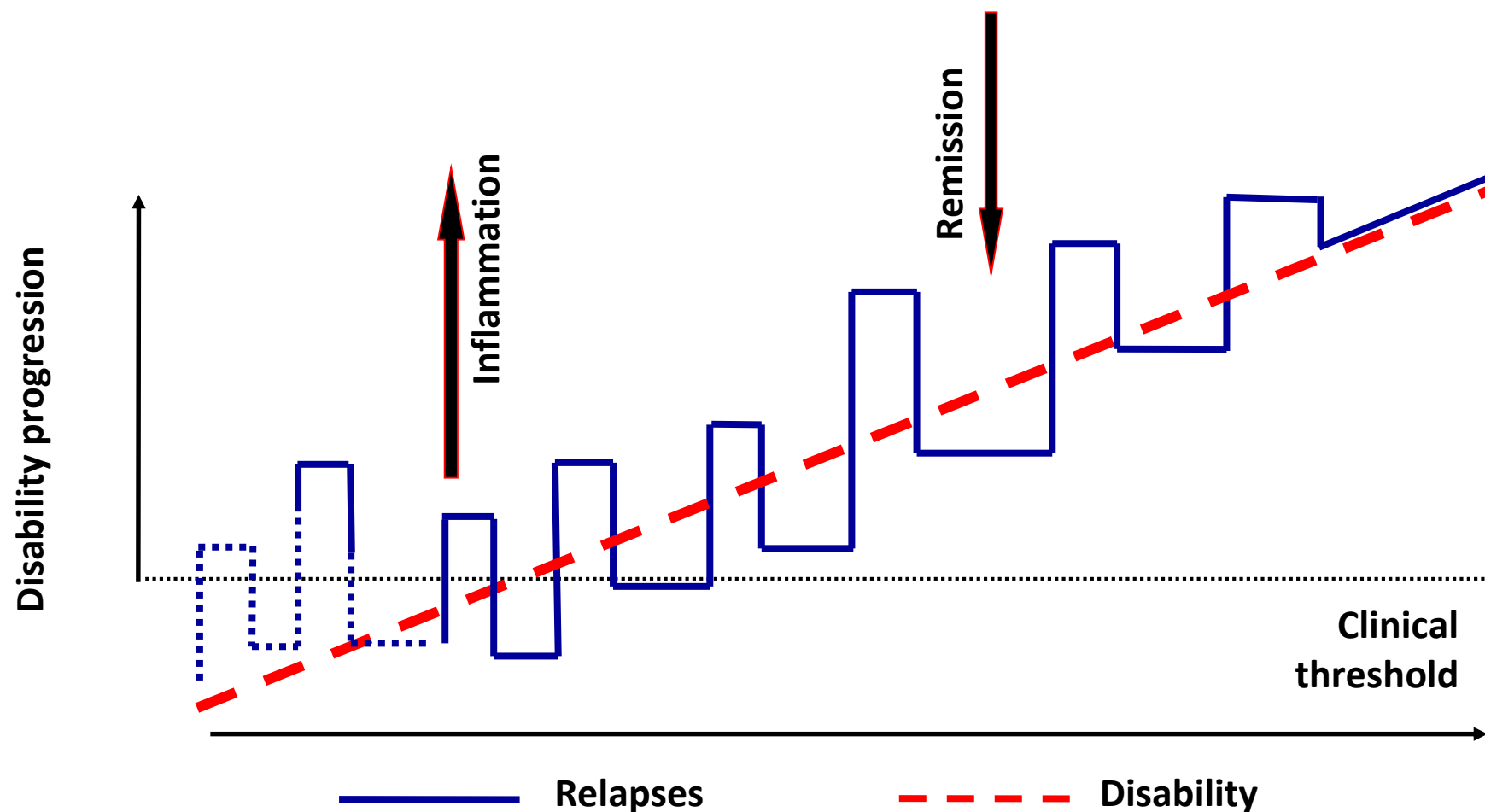
LEARN MORE ON

MS MultipleSclerosis.net

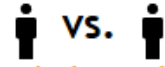
Arrow Project Study

- Aim: **Assess cytokines profile in acute multiple sclerosis relapses:**
- Sample size calculation
- Student role:
 - Characterize relapse time pattern
 - Prediction of clinical relapse outcome

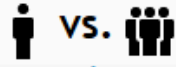
The time pattern of acute MS relapse



Study Group Design



Two independent
study groups



One study group
vs. population

Two study groups will each receive different treatments.

Primary Endpoint



Dichotomous
(yes/no)



Continuous
(means)

The primary endpoint is **binomial** - only two possible outcomes.
Eg, mortality (dead/not dead), pregnant (pregnant/not)

Statistical Parameters

Anticipated Means

Group 1 ?

10 ± 30

Group 2 ?

20

Mean

Enrollment ratio ?

1

Type I/II Error Rate

Alpha ?

0.001

Power ?

80%

Reset

Calculate

Continuous Endpoint, Two Independent Sample Study

Sample Size	
Group 1	307
Group 2	307
Total	614

Study Parameters	
Mean, group 1	10
Mean, group 2	20
Alpha	0.001
Beta	0.2
Power	0.8

$$k = \frac{n_2}{n_1} = 1$$

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2/K)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

$$n_1 = \frac{(30^2 + 30^2/1)(3.29 + 0.84)^2}{10^2}$$

$$n_1 = 307$$

$$n_2 = K * n_1 = 307$$

$\Delta = |\mu_2 - \mu_1|$ = absolute difference between two means

σ_1, σ_2 = variance of mean #1 and #2

n_1 = sample size for group #1

n_2 = sample size for group #2

α = probability of type I error (usually 0.05)

β = probability of type II error (usually 0.2)

z = critical Z value for a given α or β

k = ratio of sample size for group #2 to group #1

What is an acute relapse?

- Episodes of acute neurologic function disturbances.

- Lasting longer than 24 hours.



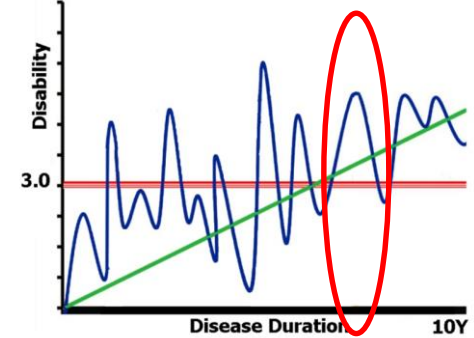
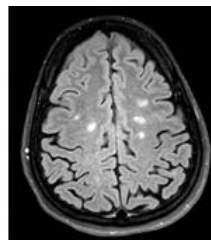
- Followed by a full recovery (or residual deficits) of at least 30 days.



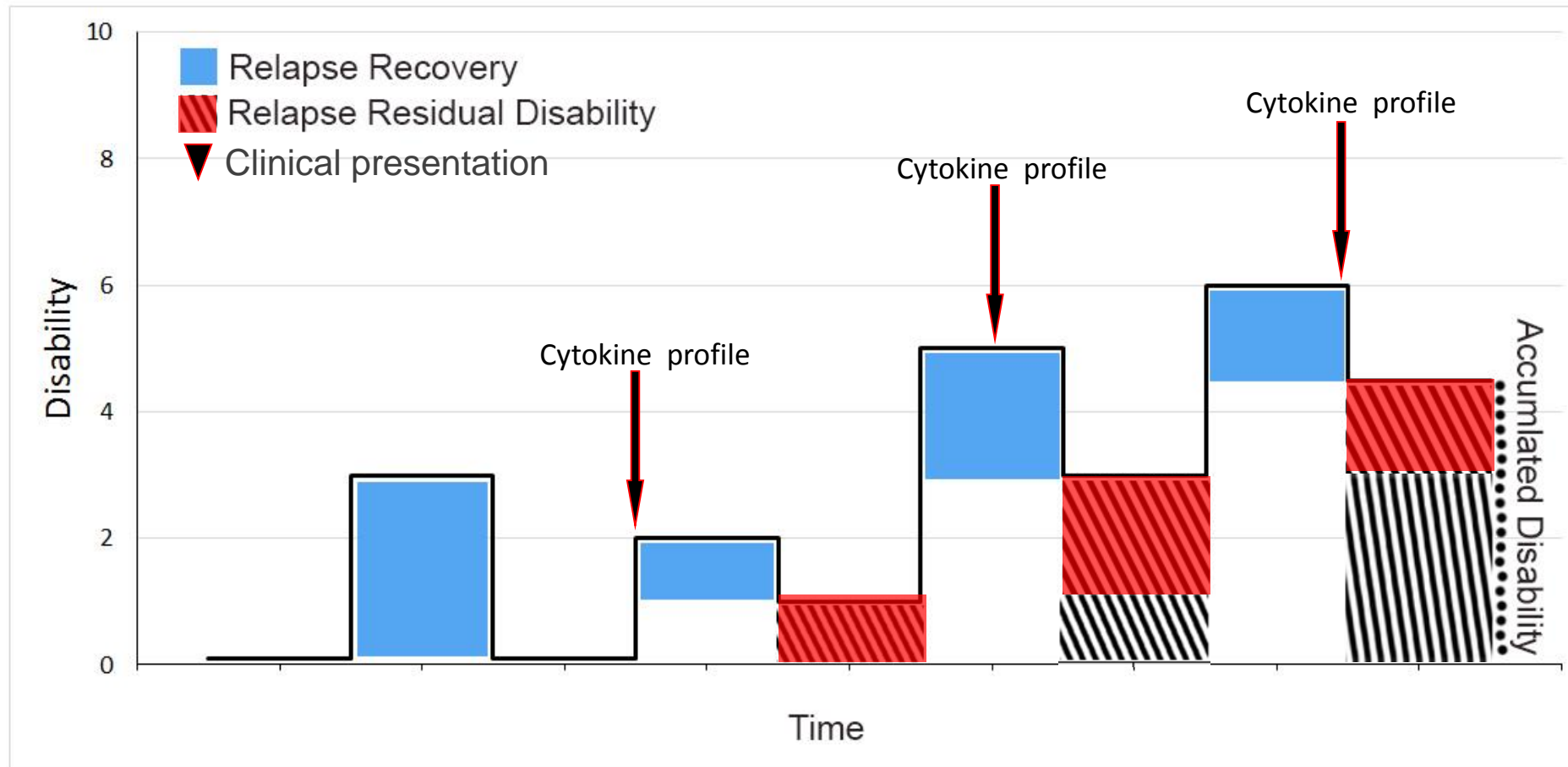
- Periods between disease relapses characterized by a lack of disease progression.



- The disease is defined as 'active' in the presence of relapses and/or evidence of new MRI activity.



Acute relapses are the major cause that determines disease activity and future disability



[illegible]

מסך ראשי

טופלים פעילים: 4365
ת.ז. עם ספרת ביקורת

מטופל:

סוג ארוע
ביקור
04/09/2018
ת.ביקור
CDMS A1 ודאני מערי

בדיקות מעבדה

שם בדיקה	תוצאה מלל	חריגה	בדיקה	ת.בדיקה	ערך מינ	ערך מקס	הערה F5	ת. רישום
Interferon gamma	19.160		14104	22/01/2018	0.00	30.00		23/01/2018
IL-10	17.290	HIGH	14104	22/01/2018	0.00	15.00		23/01/2018
IL-12	7.460		14104	22/01/2018	0.00	10.00		23/01/2018
IL-17	16.600		14104	22/01/2018	0.00	25.00		23/01/2018
Interferon gamma	20.710		13154	20/04/2017	0.00	30.00		20/04/2017
IL-10	14.690		13154	20/04/2017	0.00	15.00		20/04/2017
IL-12	3.770		13154	20/04/2017	0.00	10.00		20/04/2017

קבוצות
Cytokines
Cytokines-mRNA
Inflammatory markers
JCV antibodies-New

מס' בדיקה:

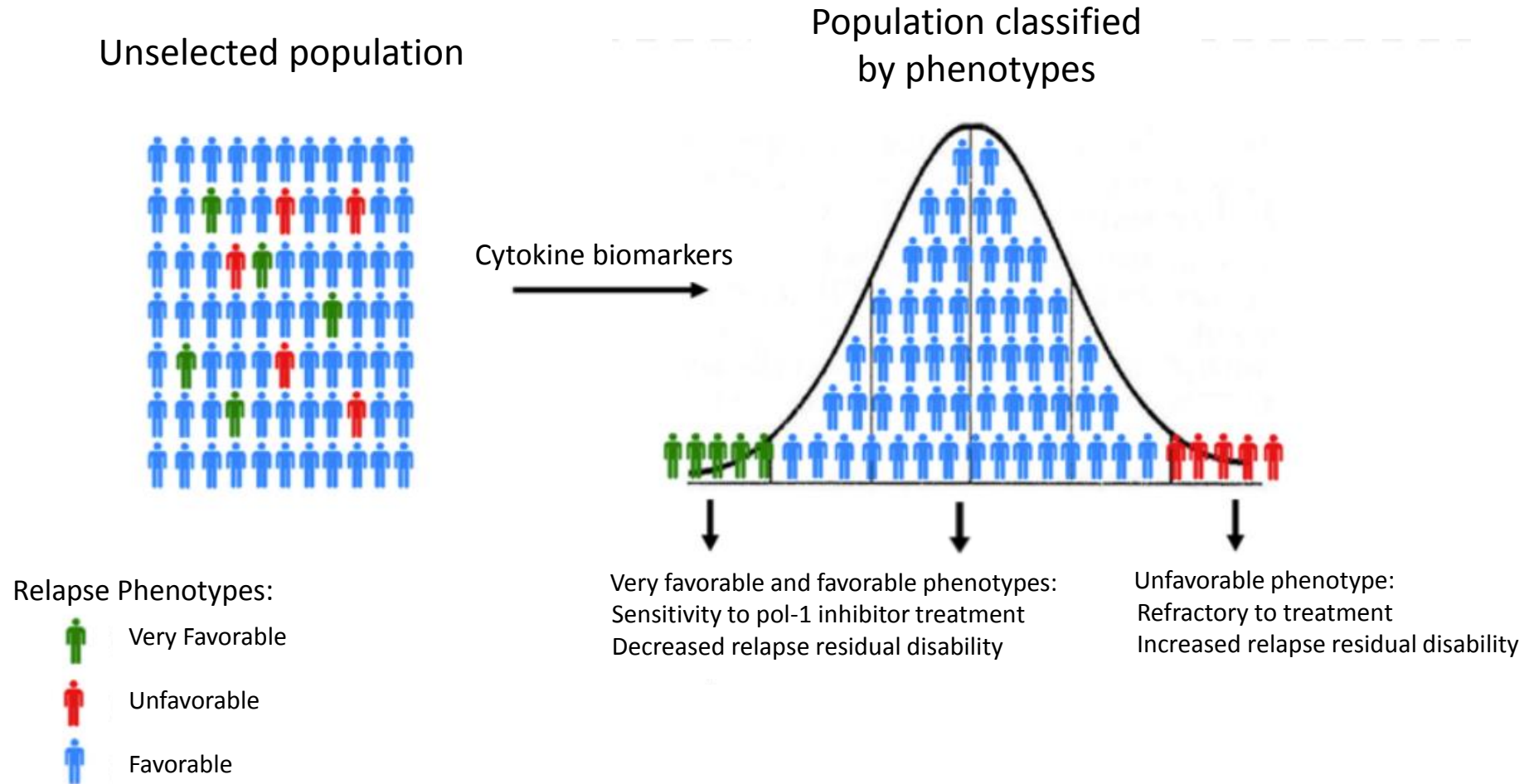
מחק בדיקות
ללא תוצאהמחק
בדיקהגרף
IMDMגרף
inflammatoryטקסט גרף
inflammatoryיישום DNA הדפסה יציאה
בדיקות

Trying to find a pattern

- The relationship between cytokines in the acute relapse setting.
- Is there a correlation between which cytokines are elevated and the course of the relapse?
- Is there a correlation between certain cytokines or their levels to the severity of the relapse?



Prediction of Acute relapse outcome by cytokine-related biomarkers



THANK
YOU!

