

# War stress, psychological coping mechanisms and exacerbations of Multiple Sclerosis

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“...But the circumstances most commonly assigned as causes of this disease, by patients, appertain to the moral order – long continued **grief or vexation**, such as may arise from illicit pregnancy or the annoyances which a **false social position** entails. Male sufferers are for the most part, persons who have **lost caste**, thrown out of the general current and **ill provided with the means of maintaining the struggle for life...**”

**J.M Charcot,**

*“Lectures on the diseases of the nervous system”,*

Lecture VIII: **Disseminated Sclerosis, 1879.**



The relationship of MS to physical trauma and psychological stress: Report of the  
Therapeutics and Technology Assessment Subcommittee of the American Academy of  
Neurology

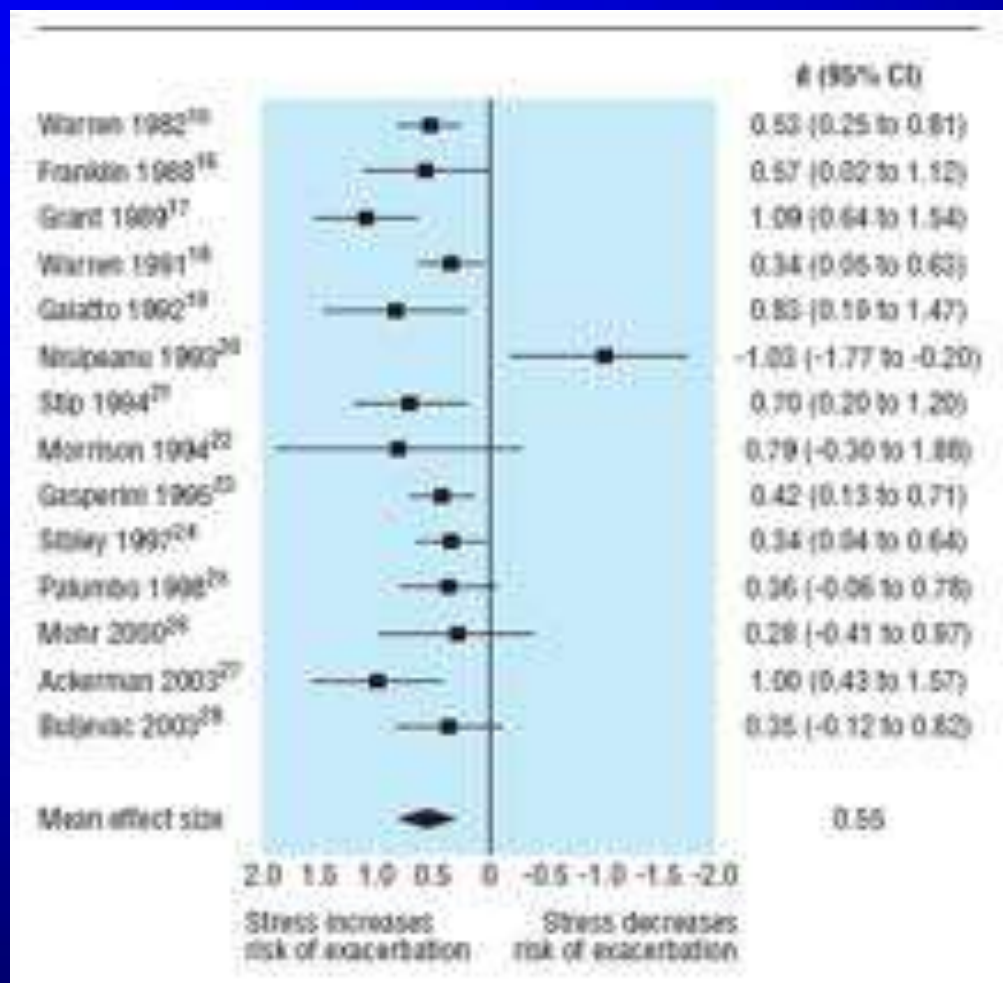
D. S. Goodin, G. C. Ebers, K. P. Johnson, M. Rodriguez, W. A. Sibley and J. S. Wolinsky  
*Neurology* 1999;52;1737-48

- “The relationship between antecedent **psychological stress** and MS exacerbation is **considered possible**. Nevertheless, the existing studies have important limitations and the prospective data are insufficient “.
- “Any posited association of trauma with more than a small effect on MS exacerbation is excluded. The preponderance of evidence supports **no association** between **physical trauma** and either MS onset or exacerbation”.

# Association between stressful life events and exacerbation in multiple sclerosis: a meta-analysis

David C Mohr, Stacey L Hart, Laura Julian, Darcy Cox and Daniel Pelletier

*BMJ* 2004;328:731-; originally published online 19 Mar 2004;  
doi:10.1136/bmj.38041.724421.55



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# Psychological stress as risk factor for exacerbations in multiple sclerosis

P. Nisipeanu, MD, and A.D. Korczyn, MD, MSc

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**Article abstract**—We prospectively evaluated the relationship between a common psychological stressor and relapses in multiple sclerosis (MS) in a group of 32 MS patients exposed to the threat of missile attacks during the Persian Gulf War of 1991. The number of relapses during the war and the following 2 months was significantly lower than expected based on the frequency during the preceding 2 years, suggesting that not all stress conditions increase the risk of exacerbations in MS.

NEUROLOGY 1993;43:1311-1312

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# Aims

- To assess the relation between war stress due to the rocket attacks on northern Israel during the second Lebanon war and MS exacerbations.
- To study the influence of various psychological coping strategies with stress on disease relapses.



# Methods

- 156 patients with relapsing-remitting MS
- All residents of northern Israel
- All under regular follow up by our clinic
- We compared the number of severe relapses during the 34 days of the war and during the 3 months following the war - to similar time periods at the preceding year.

# Methods

- We used structured interviews using questionnaires previously validated to measure:

- Subjective feeling of distress .

Perceived Stress Scale [ J health Soc Behav 1983; 24: 385-396 ]

- Subjective stress due to specific war events .

Harvard Trauma Questionnaire [ [www.hpvt-cambridge.org](http://www.hpvt-cambridge.org) ]

- Psychological coping strategies with stress .

“Brief COPE” [ Int J Behav Med 1997, 4: 92-100. ]

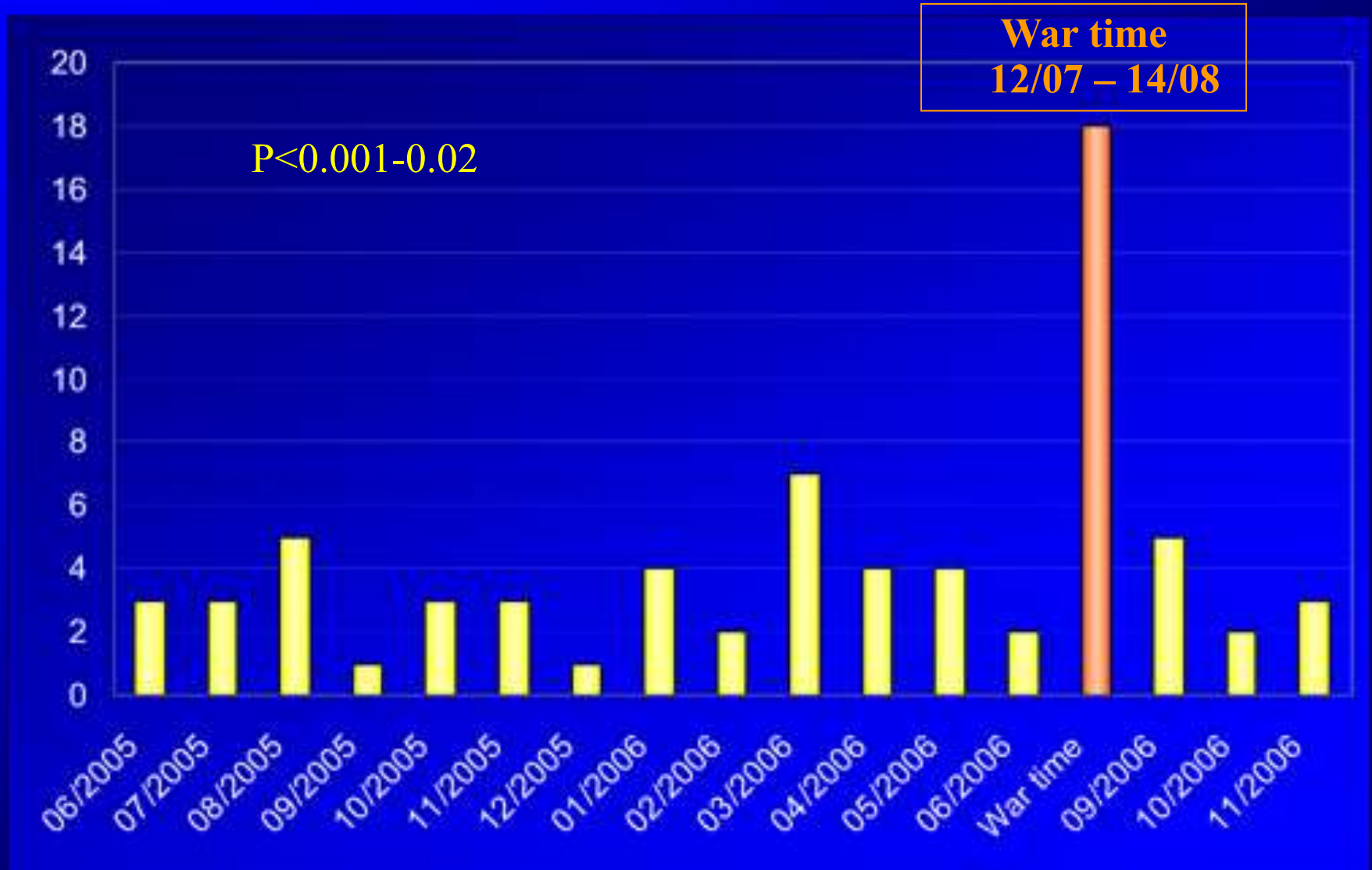
- Interviews were made during the 4th month after the war.



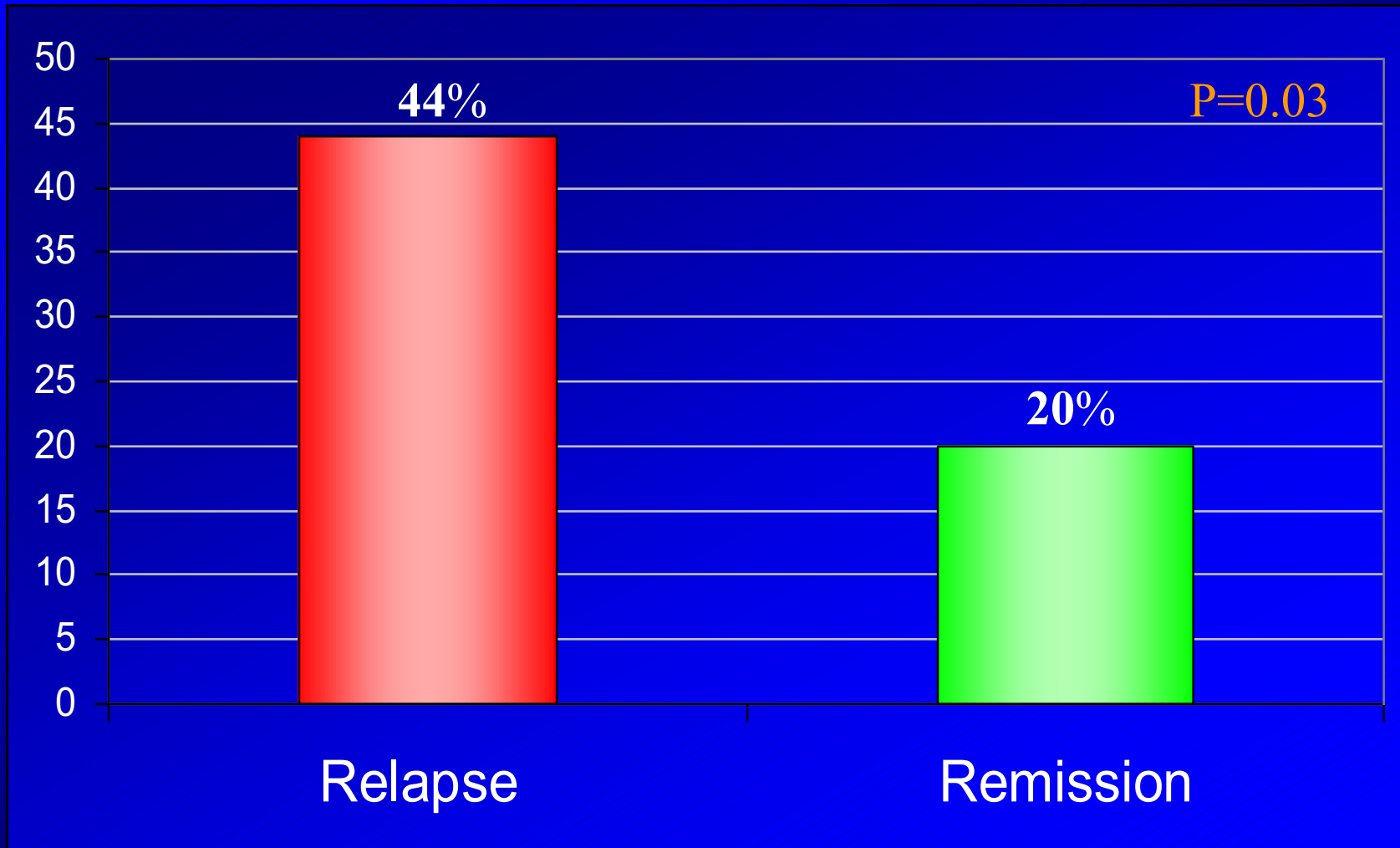
# Results

<b>N</b>		<b>156</b>
<b>Gender</b>	Women	<b>121 (78%)</b>
	Men	<b>35 (22%)</b>
<b>Age</b>	Mean $\pm$ Std (range)	<b>44 <math>\pm</math> 12 (17 – 71)</b>
<b>Duration of illness</b>	Mean $\pm$ Std (range)	<b>10 <math>\pm</math> 7 (1 – 35)</b>
<b>EDSS</b>	Mean $\pm$ Std (range)	<b>2.8 <math>\pm</math> 1.8 (0 – 6.5)</b>
<b>Relapses 6/05 – 6/06</b>	None	<b>128 (82%)</b>
	One	<b>18 (12%)</b>
	2-4 relapses	<b>10 (6%)</b>
<b>Disease modifying drugs</b>	Number (percent)	<b>126 (81%)</b>
<b>Stayed home during the war</b>	At least few days	<b>144 (92%)</b>
	More than 1 week	<b>120 (77%)</b>

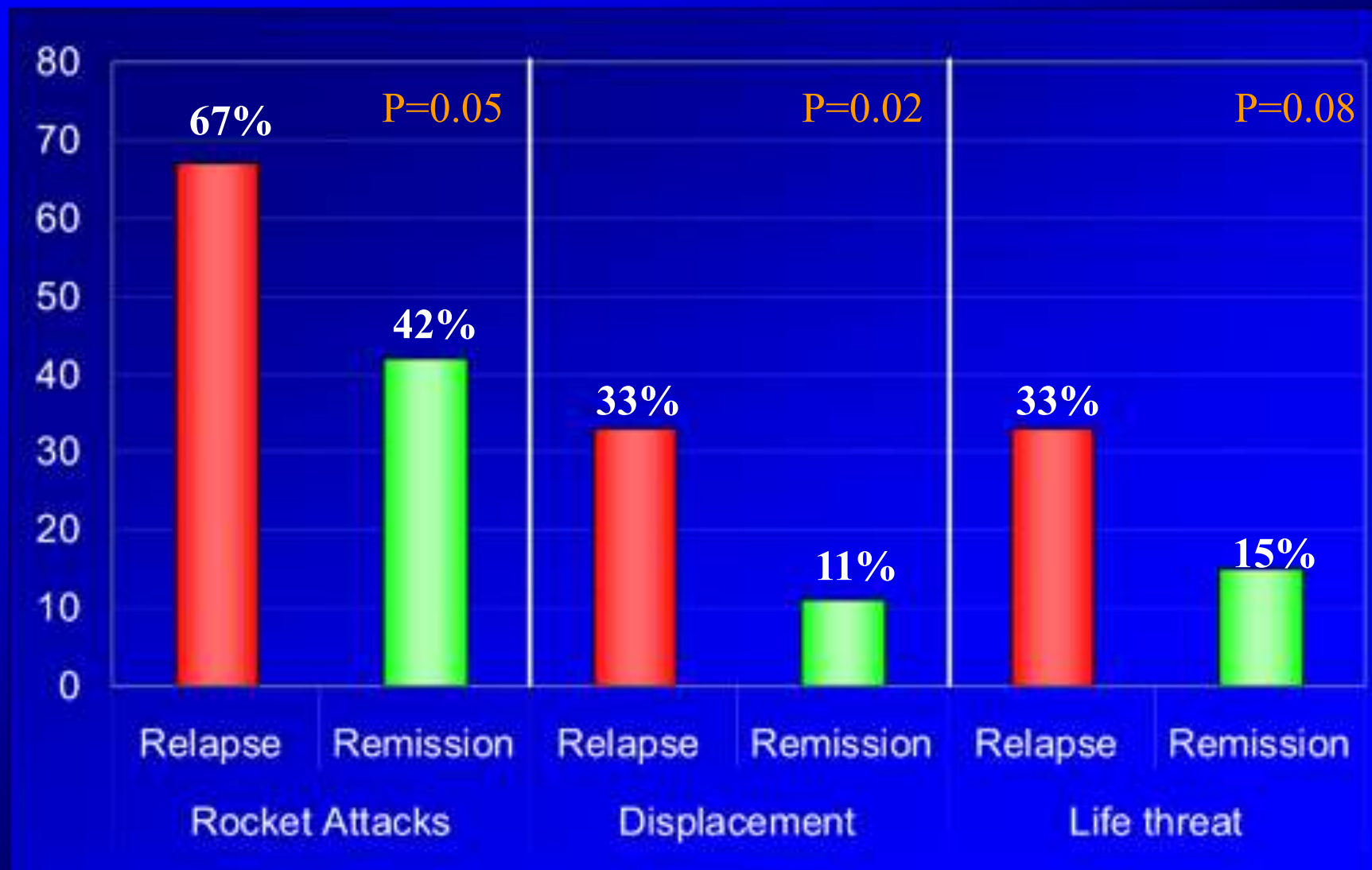
# Number of severe relapses per month



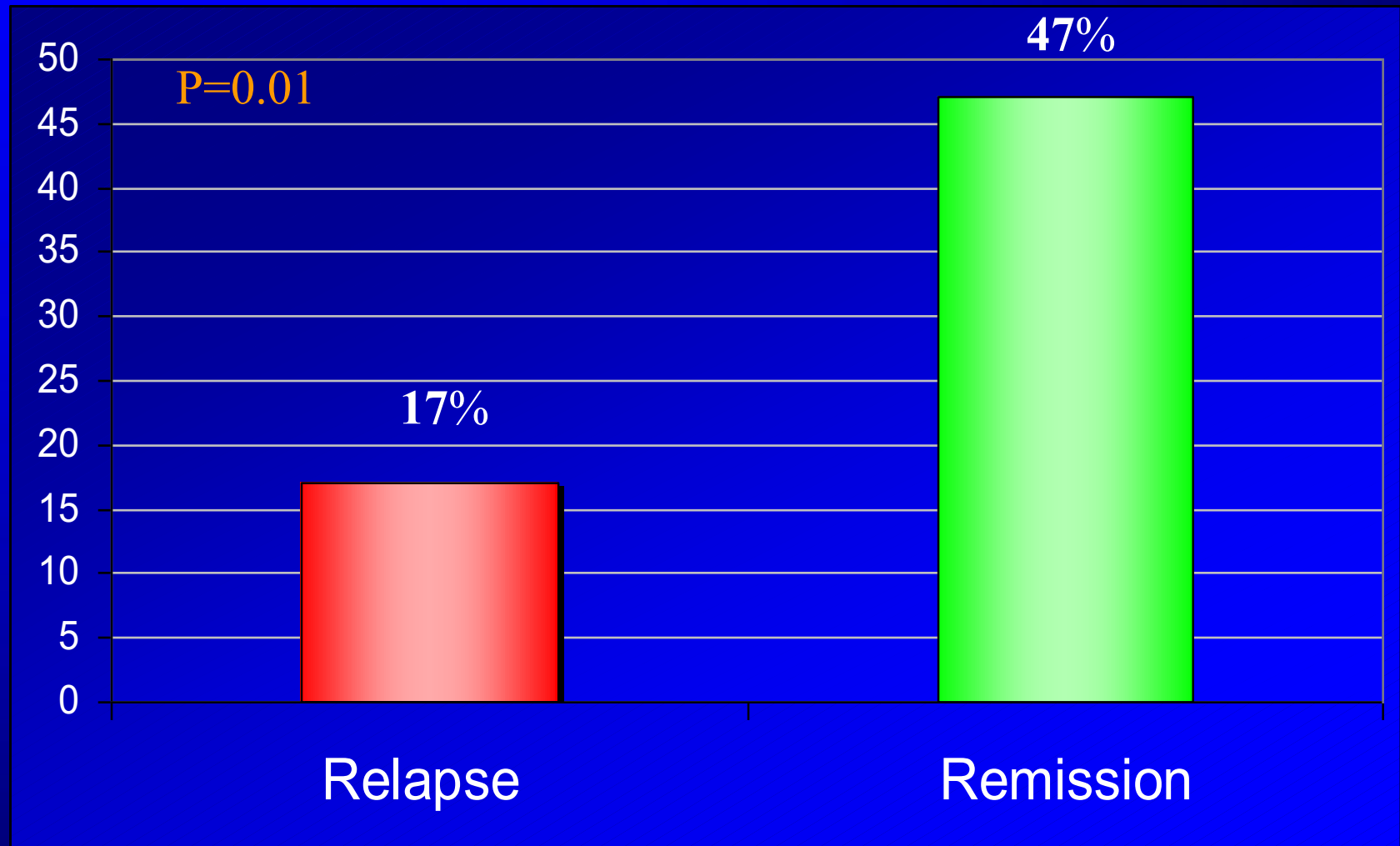
# Percent with high scores on the Perceived Subjective Stress Scale



# Proportion of patients reporting high levels of distress associated with specific war events



# Percent using “Active coping” and “Planning”



# Predictors of war-time relapse by a logistic regression model

Subjective sense of stress	O.R=3.35, 95% C.I: 1.01-11.03
Distress associated with displacement	O.R=5.1, 95% C.I: 1.3 - 19.7
MS relapse in previous year	O.R=2.05, 95% C.I: 1.05 - 4.01
Active coping and planning	O.R=0.1, 95% C.I: 0.02 - 0.5

$$R^2 = 0.26$$

# Relation to previous studies

- Our results further support the association between psychological stress and MS exacerbations, in line with most previous studies.
- Our results confirm the beneficial role of problem solving coping strategies in multiple sclerosis

*J Psychosom Res, 1991; 35: 37-47*

*Psychosom Med, 2002; 64: 803-9*

*Multiple Sclerosis, 2006; 12: 465-75*



## What this study adds ?

- To the best of our knowledge, this is the first study indicating that **severe life threatening situations** (war-like) are associated with MS relapses. (Previous studies dealt with daily hassles and life difficulties of **moderate** intensity).
- Our findings suggest that increased MS relapse rate occur during times **when a stressful process is still at its peak**. (Previous clinical and MRI studies reported exacerbations to occur 2-8 weeks after stressor onset, and even more on the rebound from the stressful situation).

# Proposed biological models for the association between stress and MS relapses:

- Stress  $\rightarrow$  CRH  $\rightarrow$  ACTH  $\rightarrow$  Cortisol  $\uparrow$  .
- Stress resolution  $\rightarrow$   $\downarrow$  Cortisol  $\rightarrow$  Relapse .
- Stress  $\rightarrow$  CRH  $\rightarrow$  Mast cell activation  $\rightarrow$   
 $\uparrow$  B.B.B permeability  $\rightarrow$  Relapse .

# Conclusions

- War stress is associated with increased risk of MS exacerbation .
- Problem solving coping strategies potentially reduce this risk.
- These findings suggest potential role for preventive interventions tailored for MS patients at-risk .

# Many thanks

Sara Dishon

Limor Cuzin-Disegni

Idit Lavi

Eli Somer

Ariel Miller

