Physical activity:
‘Is sweat the best antidepressant?’

Guy Faulkner, PhD

UNIVERSITY OF TORONTO
FACULTY OF PHYSICAL EDUCATION AND HEALTH

The problem of mental health

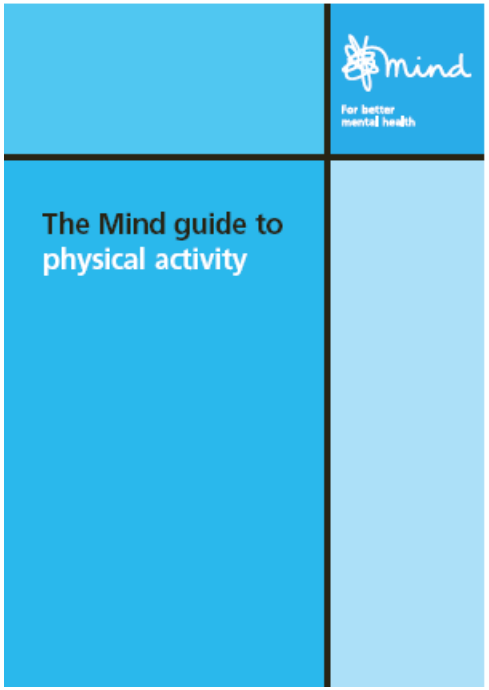
Mental health problems:-

- widespread
  - 1 in 5
- increasing
  - 18.2% in 1994-1995 to 32.6% in 1998-1999 receiving antidepressants in Canada (Patten, 2002)
- expensive
  - $7.331 billion in 1993

Health Canada. *A Report on Mental Illnesses in Canada*. Ottawa, Canada 2002

Physical Activity Promotion in the Mental Health Field

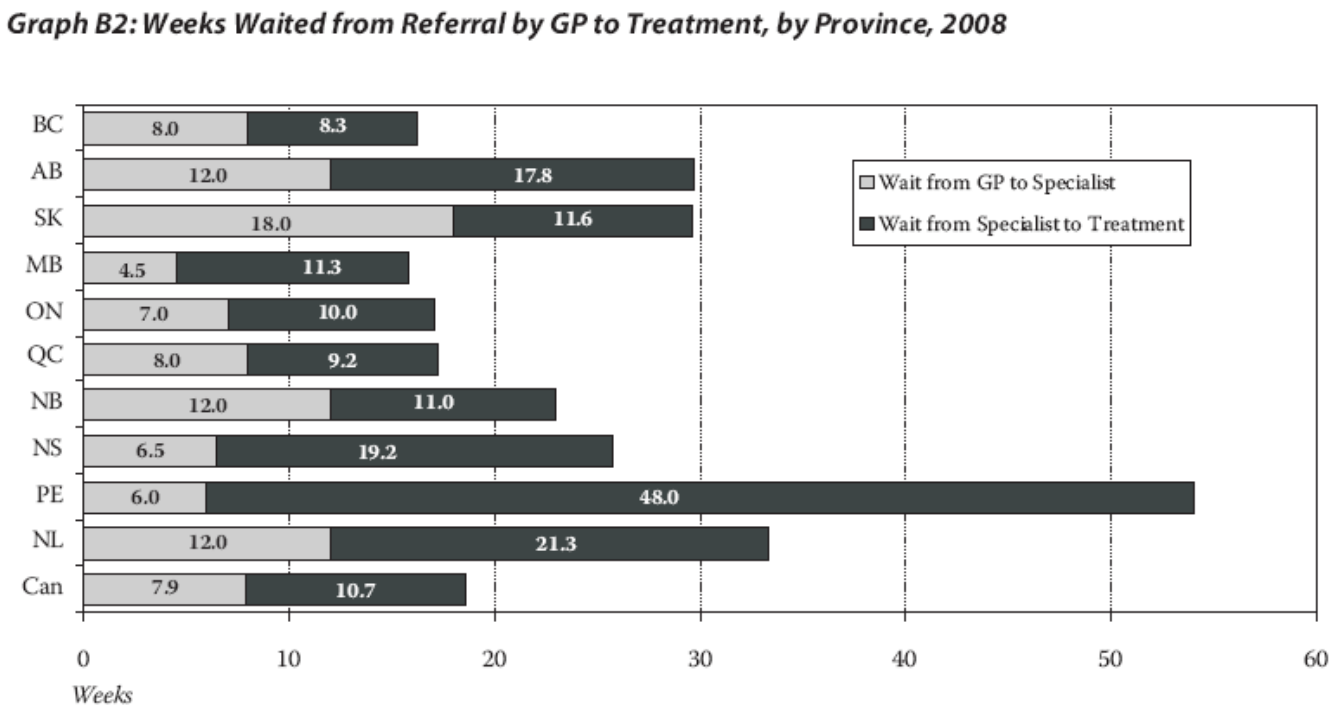
- Significant and severe co-morbid conditions experienced by people with mental illnesses that lead to secondary disability and premature death
- Philosophical change in health care: Illness to wellness
- Service user advocacy



Advantages of Physical Activity?

- Cheap
- No negative side-effects
- Potentially far reaching
- Self-administered

Psychiatric Treatment in Canada

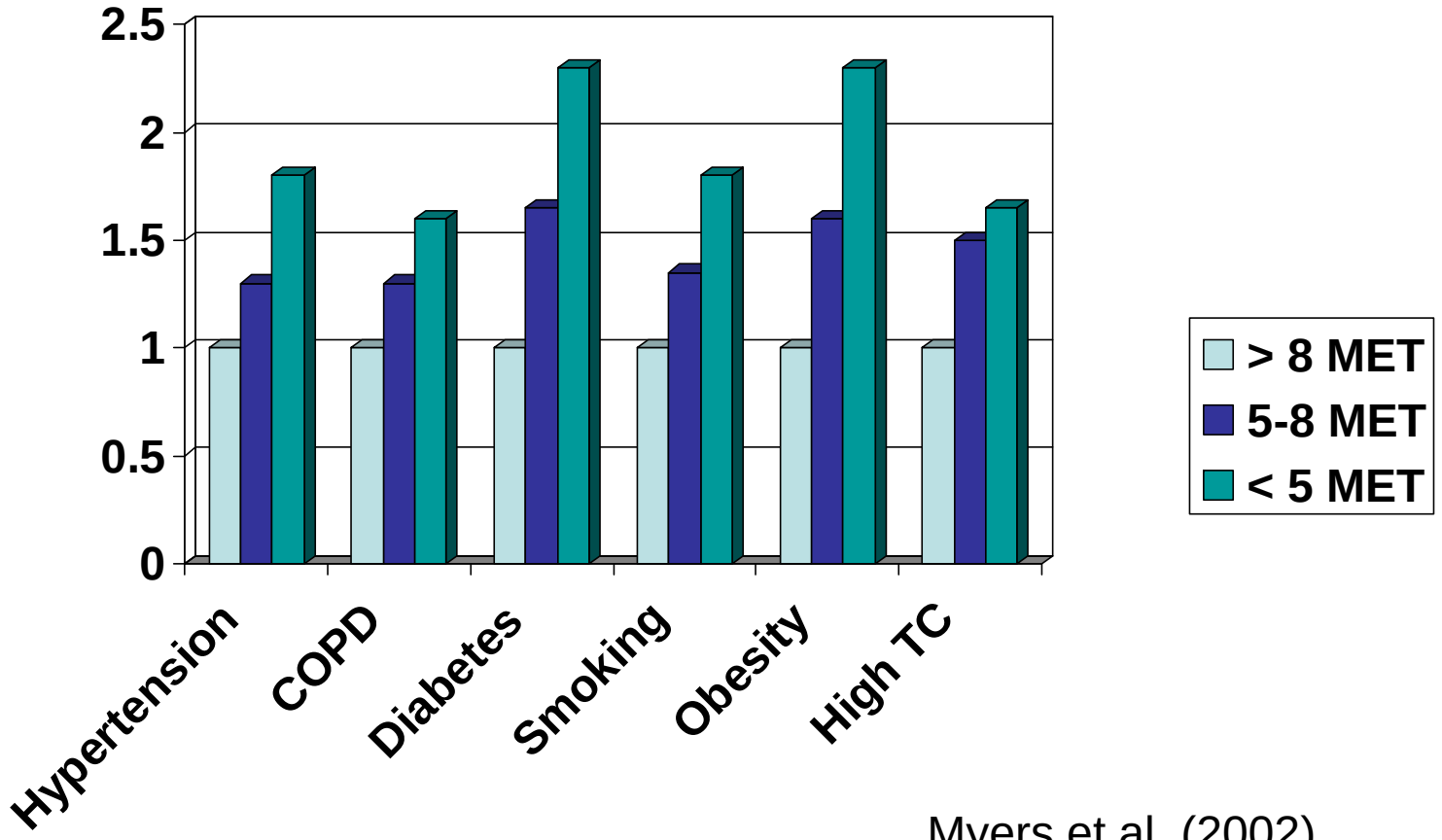


Waiting Your Turn: Hospital Waiting Lists in Canada, 2008 Report
www.fraserinstitute.org

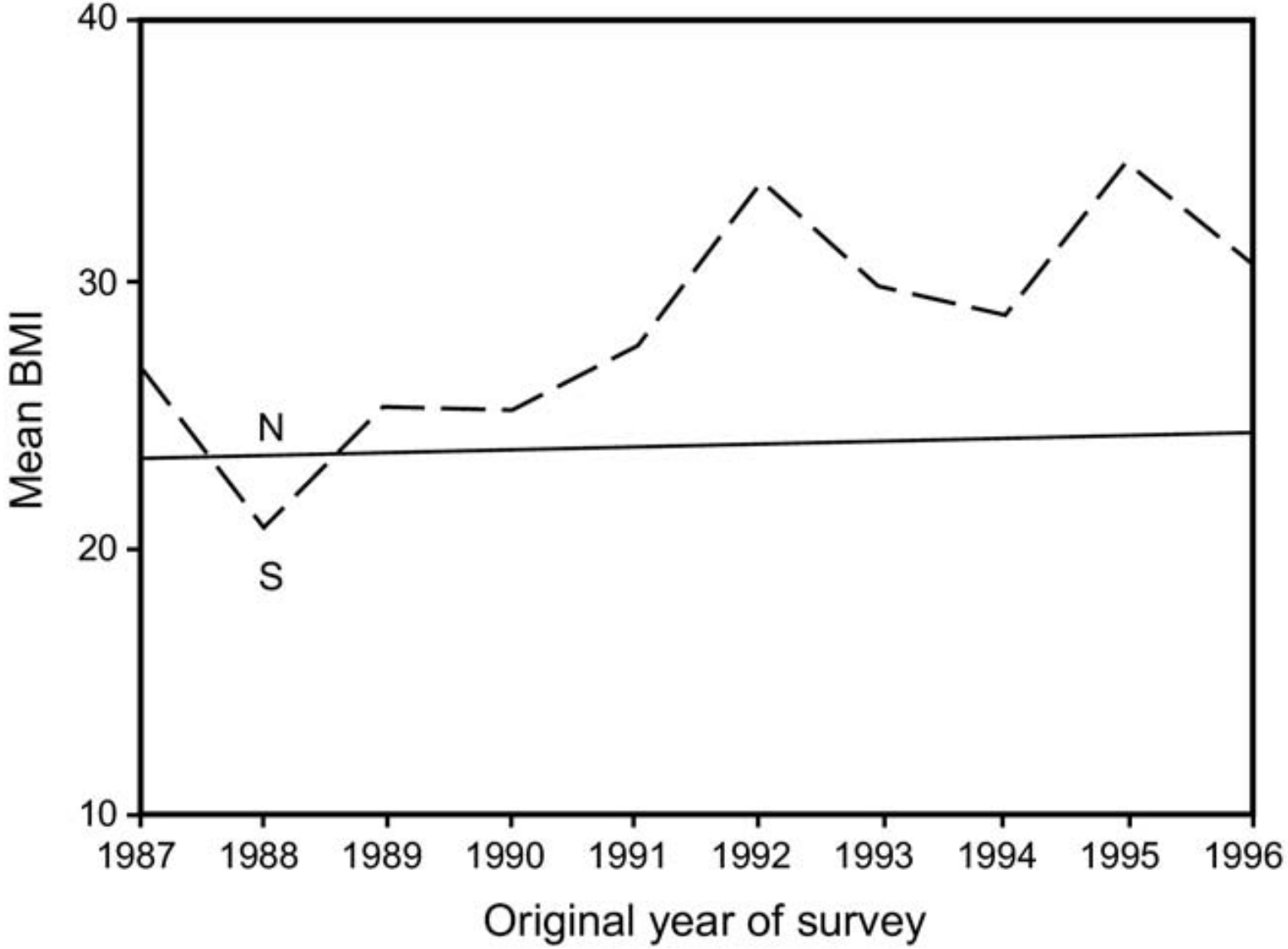
Advantages of Physical Activity?

- Cheap
- No negative side-effects
- Potentially far reaching
- Self-administered
- Physical health benefits

Exercise Capacity & Mortality

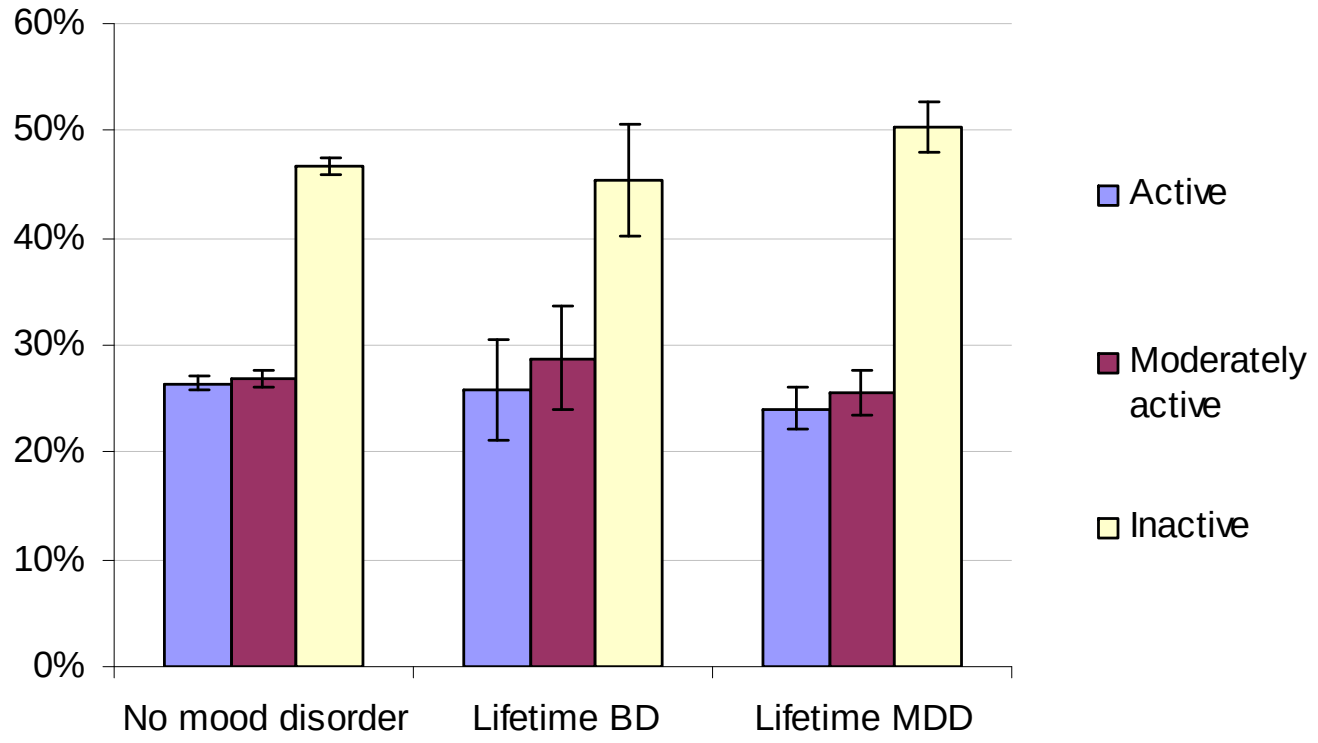


Myers et al. (2002)



Weight gain for women aged 18–30 years from 1987 to 1996 (Control [solid line] and with Schizophrenia (Homel et al., 2002)

Percentage of Respondents Reporting Active, Moderate and Inactive Levels of Physical Activity (n=36,773)



CCHS 1.2 (2002)

Exercise causes a reduction in depression

Major depressive disorder is characterized by one or more major depressive episodes (at least 2 weeks of depressed mood or loss of interest in usual activities accompanied by at least four additional symptoms of depression).

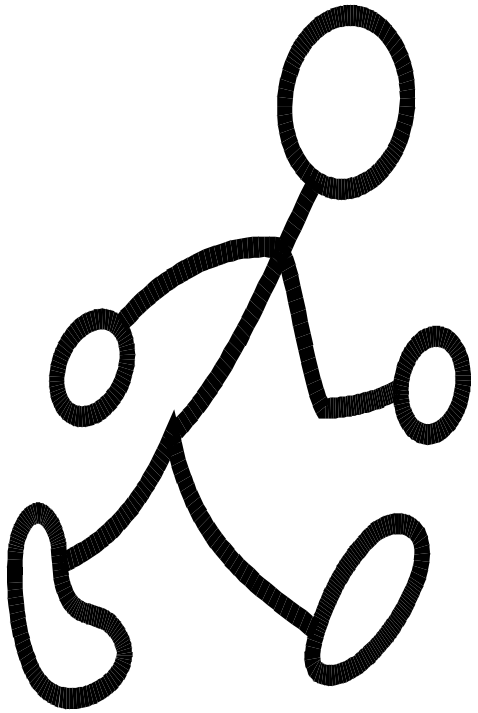
is there evidence for a causal link?

Hill, A. B. (1965). The environment and disease: Association or causation? Proceedings of the Royal Society of Medicine, 58, 295-300.

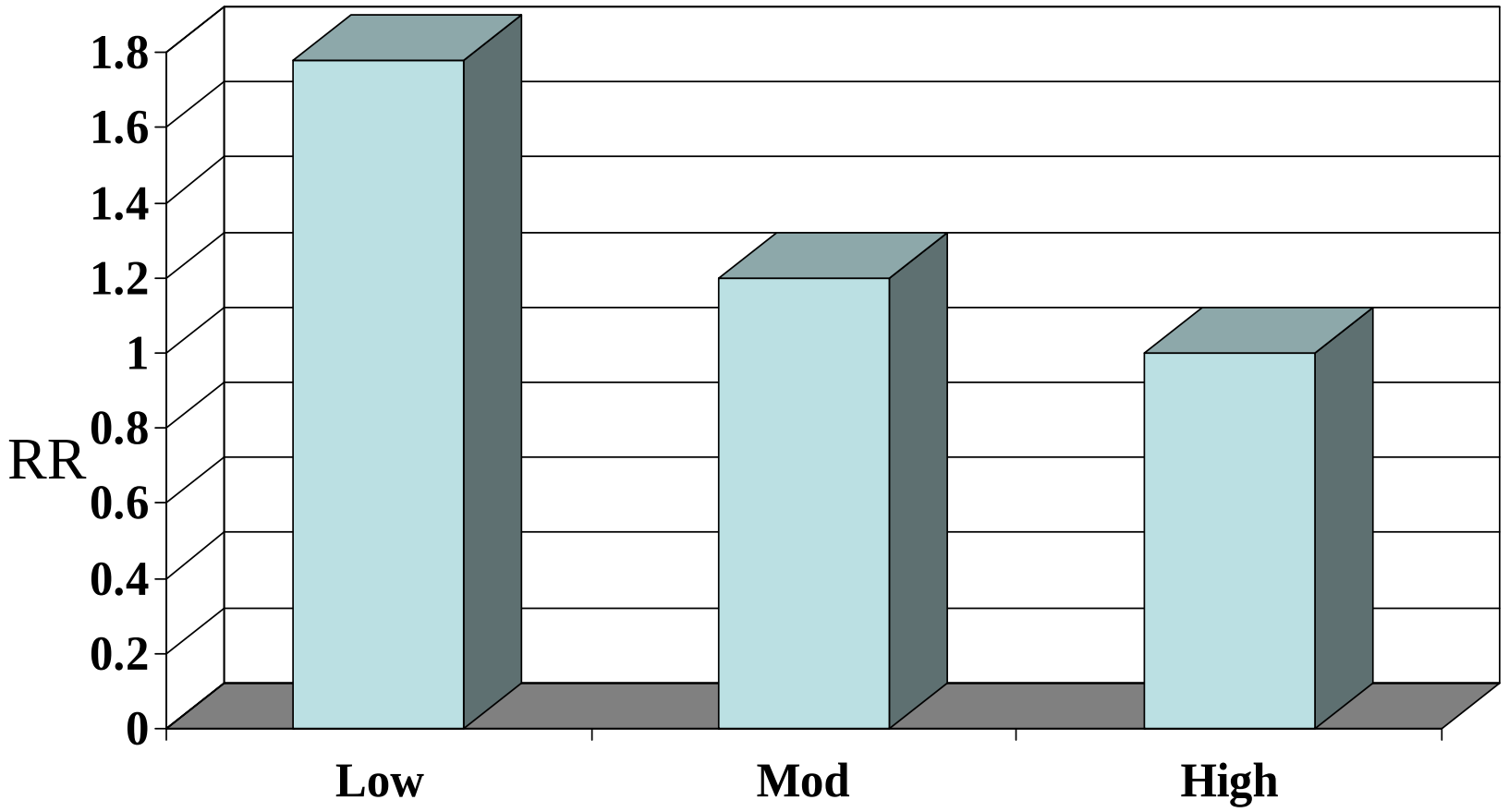
- temporal sequence
- strength of association
- consistency
- experimental evidence
- dose response
- coherence
- specificity
- biological plausibility

Evidence for the role of PA and exercise in prevention and treatment of clinically defined depression

- Temporal sequencing
  - – The most critical of the criteria for epidemiological data
  - – cross-sectional data are insufficient evidence



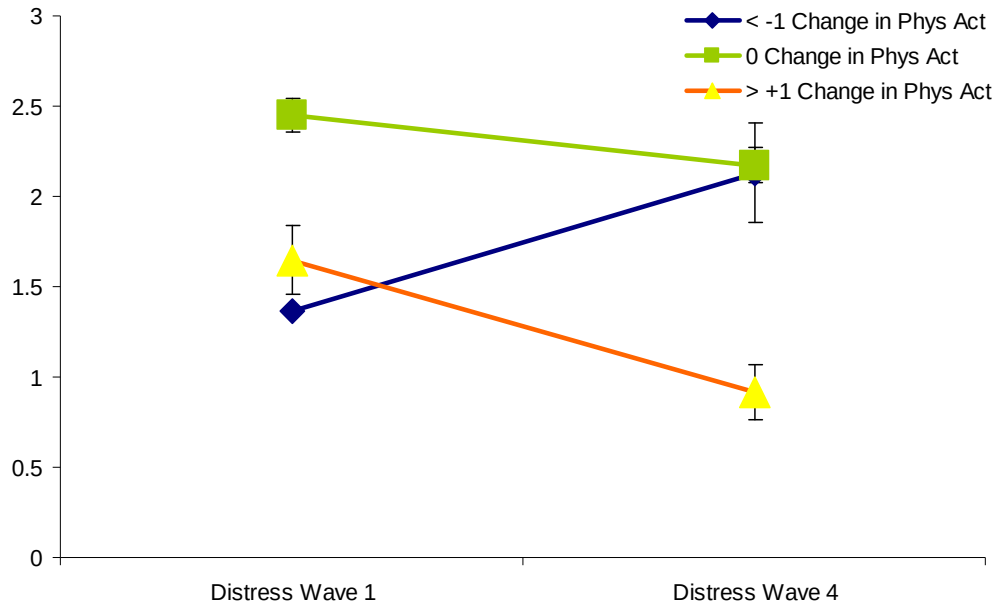
Relative risk of depression: 10 year follow-up



PA at baseline

[Camacho et al., 1991]

Changes over time in Physical Activity and Psychological Distress among Older Adults



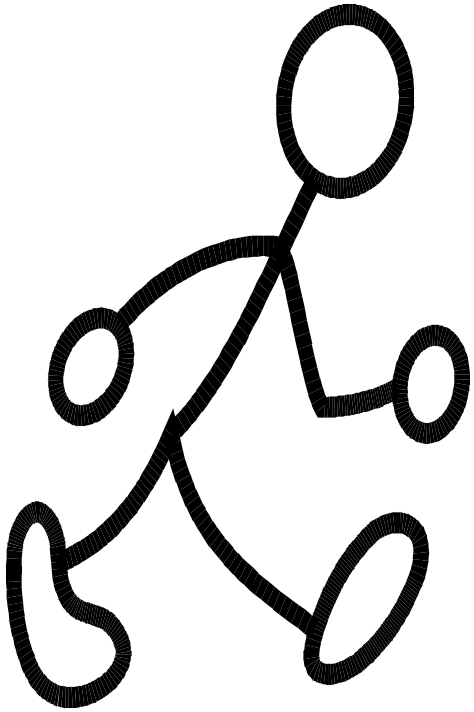
Cairney, J., Faulkner, G., Veldhuizen, S., & Wade, T.J. (2009). Physical activity and psychological distress in older adults: A longitudinal analysis. *Canadian Journal of Psychiatry*, 54,160-9.

Temporal sequencing

- There are at least 8 epidemiological studies that can demonstrate appropriate temporal sequencing for clinical depression.
- Could these findings be explained by:
  - bias - unlikely large population studies with checks made on non-respondents
  - confounding- in all studies statistical adjustments are made for disability, BMI, smoking, alcohol, social status

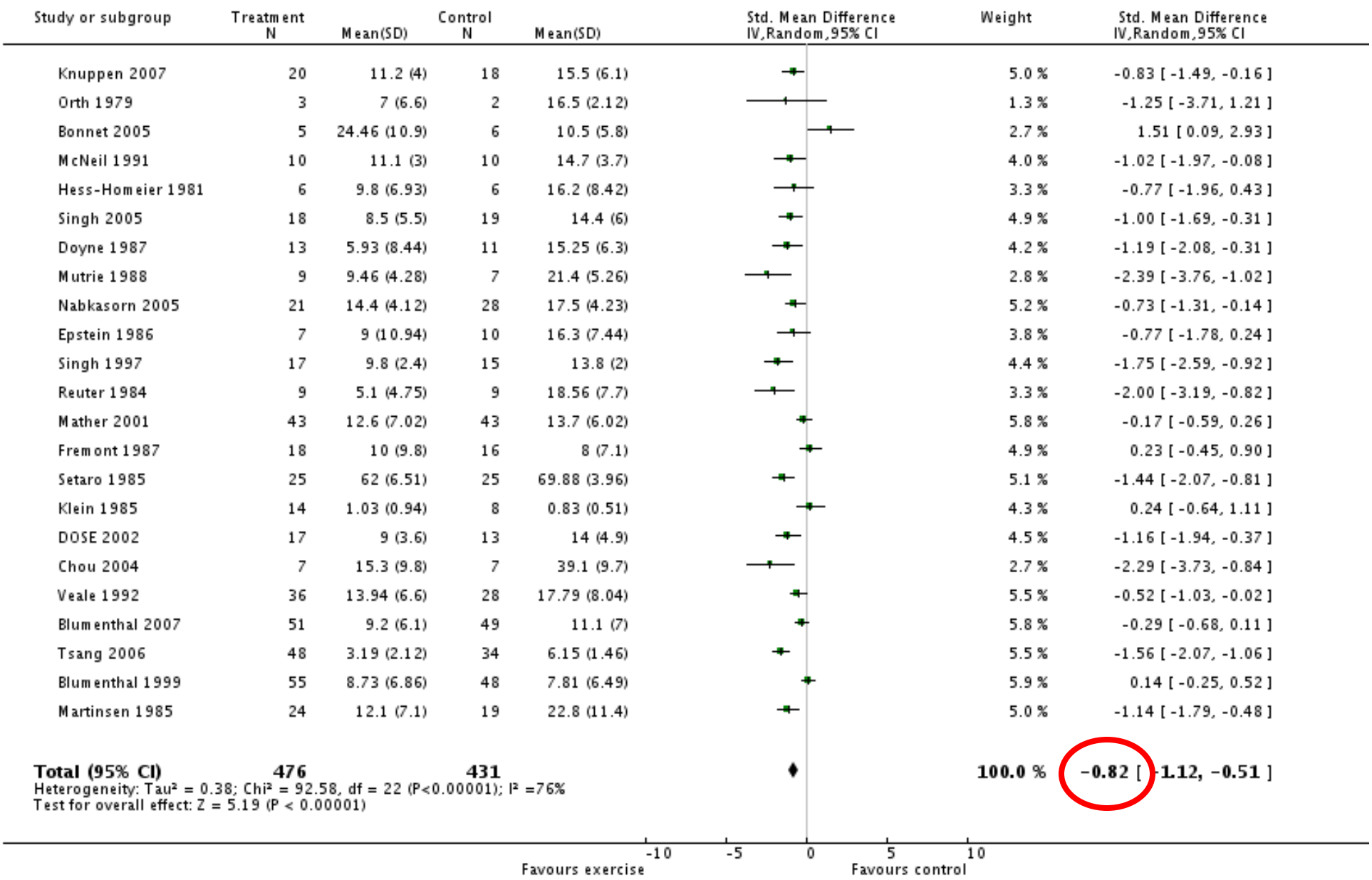
Evidence for the role of PA and exercise in prevention and treatment of clinically defined depression

- Strength of association
  - epidemiological evidence suggests a twofold risk of developing depression from low activity status or ~25% reduction in risk if active
  - evidence from meta-analyses



Mead GE, Morley W, Campbell P, Greig CA, McMurdo M, Lawlor DA. (2008). Exercise for depression. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD004366.

Review: Exercise for depression
Comparison: 1 Exercise versus control
Outcome: 1 Reduction in depression symptoms post treatment

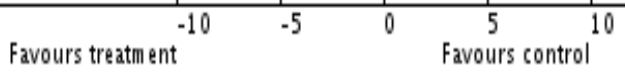


Heterogeneity: Tau² = 0.38; Chi² = 92.58, df = 22 (P<0.00001); I² =76%
Test for overall effect: Z = 5.19 (P < 0.00001)

Review: Exercise for depression
Comparison: 6 Exercise versus control: sensitivity analyses
Outcome: 5 Reduction in depression symptoms post-treatment: studies with blinded outcome assessment

Study or subgroup	Exercise N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Blumenthal 1999	55	8.73 (6.86)	48	7.81 (6.49)		18.2 %	0.14 [-0.25, 0.52]
Blumenthal 2007	53	9.2 (6.1)	49	11.1 (7)		18.2 %	-0.29 [-0.68, 0.10]
DOSE 2002	17	9 (3.6)	13	14 (4.9)		10.9 %	-1.16 [-1.94, -0.37]
Klein 1985	14	1.03 (0.94)	8	0.83 (0.51)		9.8 %	0.24 [-0.64, 1.11]
Knuppen 2007	20	11.2 (4)	18	15.5 (6.1)		12.9 %	-0.83 [-1.49, -0.16]
Mather 2001	43	12.6 (7.02)	43	13.7 (6.02)		17.5 %	-0.17 [-0.59, 0.26]
Singh 2005	18	8.5 (5.5)	19	14.4 (6)		12.5 %	-1.00 [-1.69, -0.31]
Total (95% CI)	**220**		**198**			**100.0 %**	**-0.39 [-0.75, -0.03]**

Heterogeneity: Tau² = 0.14; Chi² = 17.61, df = 6 (P = 0.01); I² =66%
Test for overall effect: Z = 2.14 (P = 0.032)



Comparison?

- Kirsch I, Deacon BJ, Huedo-Medina TB, Scoboria A, Moore TJ, et al. (2008) Initial Severity and Antidepressant Benefits: A Meta-Analysis of Data Submitted to the Food and Drug Administration. *PLoS Med* 5(2): e45.doi:10.1371/journal.pmed.0050045

Drug (Manufacturer)	Drug						Placebo				
	Protocol Number[a]	Baseline	Change	*d*	[95% CI] *d*	*N*	Baseline	Change	*d*	[95% CI] *d*	*N*
Fluoxetine (Eli Lilly and Company)	19 [27]	28.6	12.5	1.44	[0.79, 2.09]	22	28.2	5.5	0.63	[0.17, 1.10]	24
	25	26.2	7.2	0.83	[0.24, 1.41]	18	25.8	8.8	1.03	[0.50, 1.56]	24
	27 [28]	27.5	11	1.15	[0.96, 1.34]	181	28.2	8.4	0.88	[0.69, 1.06]	163
	62 (mild) [29]	17	5.89	1.02	[0.88, 1.16]	299	17.4	5.82	1.05	[0.71, 1.38]	56
	62 (moderate)	24.3	8.82	1.13	[0.98, 1.27]	297	24.3	5.69	0.72	[0.39, 1.05]	48
Venlafaxine (Wyeth Pharmaceuticals)	203 [30]	25.6	11.2	1.37	[1.19, 1.55]	231	25.3	6.7	0.82	[0.58, 1.06]	92
	301 [31,32]	25.4	13.9	1.77	[1.36, 2.17]	64	24.6	9.45	1.20	[0.91, 1.50]	78
	302 [33]	25	11.9	1.16	[0.84, 1.49]	65	24.4	8.88	0.87	[0.60, 1.14]	75
	303	23.6	10.1	1.27	[0.94, 1.59]	69	24.6	9.89	1.24	[0.94, 1.54]	79
	313 [34,35]	25.7	11	1.34	[1.16, 1.52]	227	25.4	9.49	1.15	[0.85, 1.45]	75
	206 [31,36]	28.2	14.2	1.45	[1.02, 1.89]	46	28.6	4.8	0.43	[0.12, 0.74]	47
Nefazodone (Bristol-Myers Squibb)	03A0A-003 [37]	25.4	9.57	1.15	[0.90, 1.41]	101	25.9	8	0.92	[0.59, 1.26]	52
	03A0A-004A	23.4	8.9	1.17	[0.97, 1.38]	153	23.5	8.9	1.17	[0.88, 1.47]	77
	03A0A-004B [38]	25.3	11.4	1.41	[1.18, 1.63]	156	25	9.5	1.17	[0.87, 1.47]	75
	030A2–0004 / 0005	23.4	10	1.31	[0.99, 1.63]	74	24	9.84	1.27	[0.94, 1.59]	70
	030A2–0007 [39]	25.7	12.3	1.42	[1.20, 1.63]	175	26.4	9.8	1.11	[0.74, 1.49]	47
	CN104–002	23.3	10.8	1.36	[0.99, 1.73]	57	23.1	8.2	1.03	[0.70, 1.36]	57
	CN104–005 [40]	24.5	12	1.51	[1.20, 1.83]	86	23.3	8	1.01	[0.75, 1.27]	90
	CN104–006	23.8	10	1.34	[1.03, 1.65]	80	23.5	8.9	1.20	[0.90, 1.49]	78
Paroxetine (GlaxoSmithKline)	01–001	28	13.5	1.67	[0.99, 2.34]	24	27.4	10.5	1.30	[0.71, 1.88]	24
	02–001 [41,42]	26.6	12.3	1.28	[0.89, 1.66]	51	25.9	6.8	0.70	[0.39, 1.01]	53
	02–002 [43,44]	25	10.9	1.23	[0.78, 1.69]	36	24.9	5.8	0.66	[0.27, 1.04]	34
	02–003 [45]	28.6	9.7	0.93	[0.50, 1.35]	33	28.9	7.2	0.69	[0.29, 1.08]	33
	02–004 [46]	28.9	12.7	1.87	[1.29, 2.44]	36	27.3	7.6	1.12	[0.70, 1.54]	38
	03–001 [47,48]	24.9	10.8	1.60	[1.11, 2.09]	40	24.8	4.7	0.69	[0.33, 1.06]	38
	03–002 [49,50]	24.9	8	1.14	[0.72, 1.55]	40	25.6	6.2	0.88	[0.50, 1.26]	40
				1.18	[0.76, 1.59]	41	27	10	1.19	[0.78, 1.60]	42
				1.33	[0.86, 1.79]	37	27	6.7	0.86	[0.46, 1.25]	37
				0.99	[0.60, 1.39]	40	26.8	4.1	0.41	[0.08, 0.73]	42
				1.11	[0.69, 1.52]	39	28.7	3	0.37	[0.02, 0.71]	37
				1.28	[1.15, 1.41]	403	24.5	8.2	1.14	[0.77, 1.50]	51
				0.97	[0.38, 1.57]	19	24.2	6.2	0.83	[0.31, 1.35]	22
	UK 12	22.8	9.1	1.23	[0.57, 1.88]	19	22.3	6.7	0.86	[0.00, 1.73]	10
	UK 09	26.8	8.8	0.80	[0.26, 1.35]	20	25.5	4.5	0.49	[0.01, 0.97]	21
	PAR 07	30.5	13.1	1.20	[0.38, 2.03]	13	28.3	10.9	0.99	[0.19, 1.79]	12

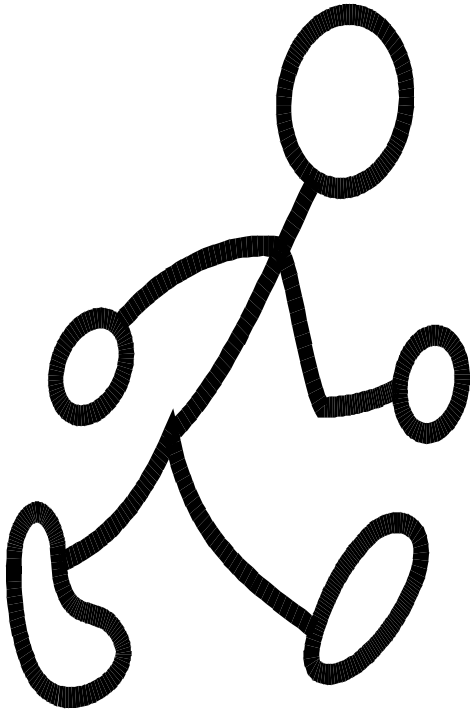
WMD = - 0.32

[a]Where available, published versions of the FDA trials are cited next to the protocol number. Citations are restricted to publications in which LOCF results were published for all sites participating in the trial. In some instances, there are minor differences in sample sizes and means between the data as submitted to the FDA and as published, and also between the data as reported for the same trial in different publications.

doi:10.1371/journal.pmed.0050045.t001

Evidence for the role of PA and exercise in prevention and treatment of clinically defined depression

- Experimental Evidence
  - At least 28 RCTs

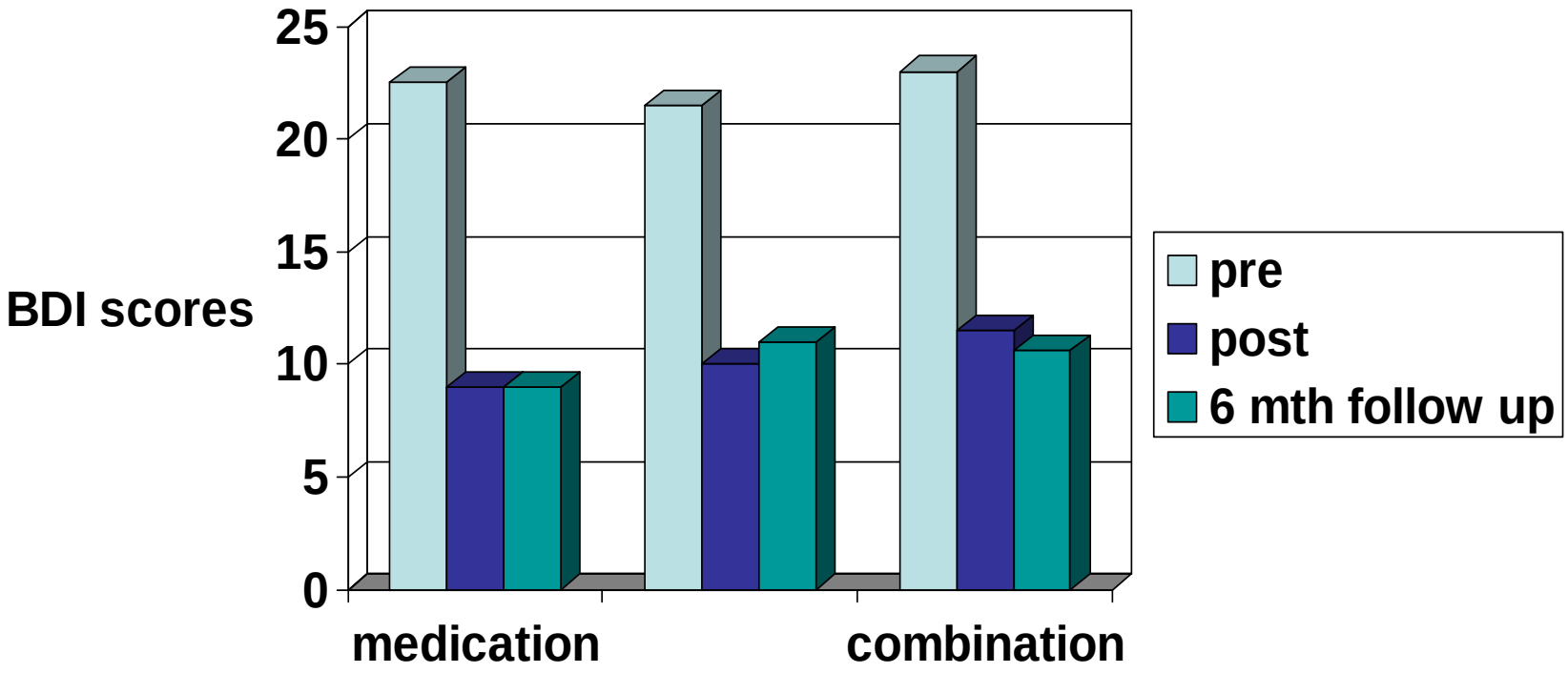


An example of an RCT

Blumenthal et al (1999) Archives of Internal Medicine, 159, 2349-56

- N = 156, aged 50-77, RCT, 16 weeks
- aerobic exercise compared to antidepressant medication or combination
- no difference between BDI scores at 16 weeks; only exercise groups improved fitness
- medication alone provided faster response

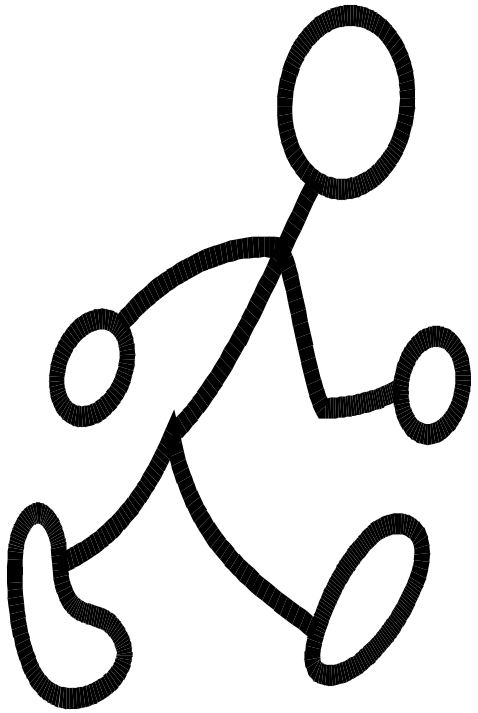
BDI scores pre and post 16 weeks of treatment (from Blumenthal et al, 1999) and 6 month follow up (Babyak et al, 2000)



Evidence for the role of PA and exercise in prevention and treatment of clinically defined depression

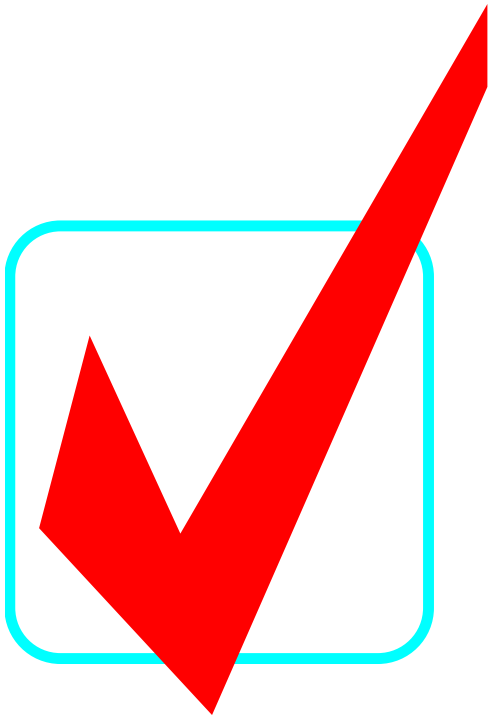
Consistency

- Different places
- Different people
- Different times
- Different circumstances



is there evidence for a causal link for depression?

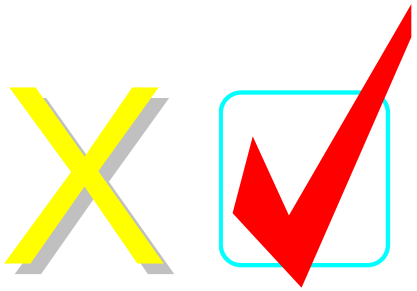
- Temporal sequence
- Strength of association
- Experimental evidence
- Consistency



What's missing?

Dose-response

- some evidence

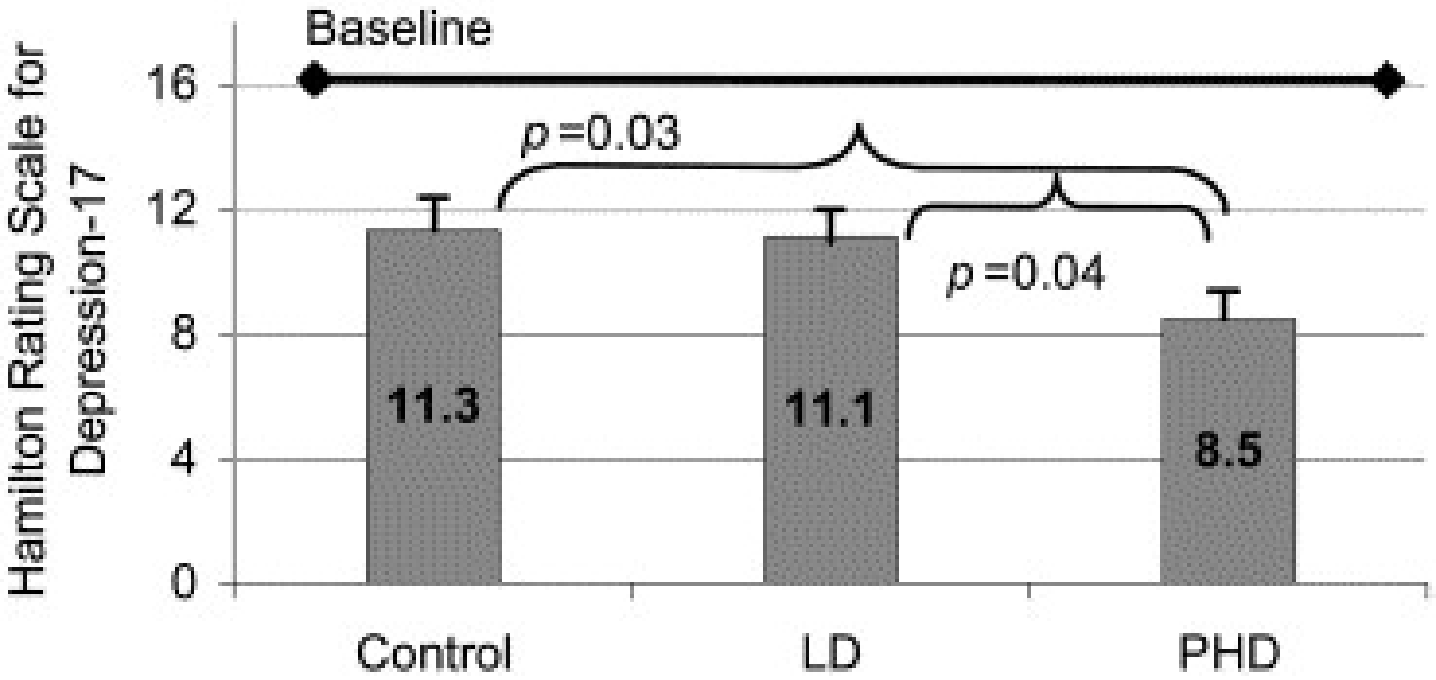


Exercise treatment for depression Efficacy and dose response

- Randomized to 1 of 4 aerobic exercise treatment groups that varied total energy expenditure (7.0 kcal/kg/week or 17.5 kcal/kg/week) and frequency (3 days/week or 5 days/week) or to exercise placebo control (3 days/week flexibility exercise) for 12 weeks.

Dunn et al. (2005), American Journal of Preventive Medicine, 28 (1), 1-8

12-week response by total energy expenditure



But what's the exercise dosage?

- What's the mechanism?
  - Individual and outcome specific
- Response may depend upon an interaction of mechanisms
- Standard exercise 'dose' unlikely to exist?

Faulkner, G. & Carless, D. (2006). Physical activity and the process of psychiatric rehabilitation: Theoretical and methodological issues. *Psychiatric Rehabilitation Journal*, 29, 258-266.

Benefits & Mechanisms: Horses for Courses

It occupies your mind, you're doing something and I don't know, it just helps me, it gives me a sense of fulfillment as well you know, if I go out for a good walk, it uses some time up, because time hangs heavy on your hands when you're not working at the moment (John)

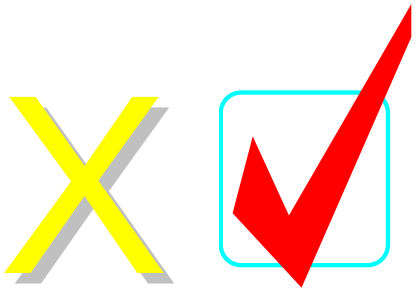
Exercise sort of enhances the sort of mind/body connection, and I think a part of depression is, you're not really in contact with your body, you're all up in your head and the thoughts going round and round. And I'd got very strong and I enjoyed feeling strong and I felt more protected feeling strong and fit And that affected my relations with other people (Peter).

Faulkner, G. & Biddle, S.J.H. (2004). Physical activity and depression: Considering contextuality and variability. *Journal of Sport and Exercise Psychology*, 26, 3-18.

What's missing?

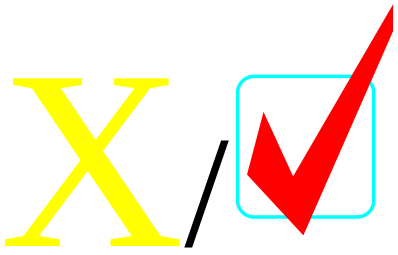
Dose-response

- some evidence
- should we expect it?



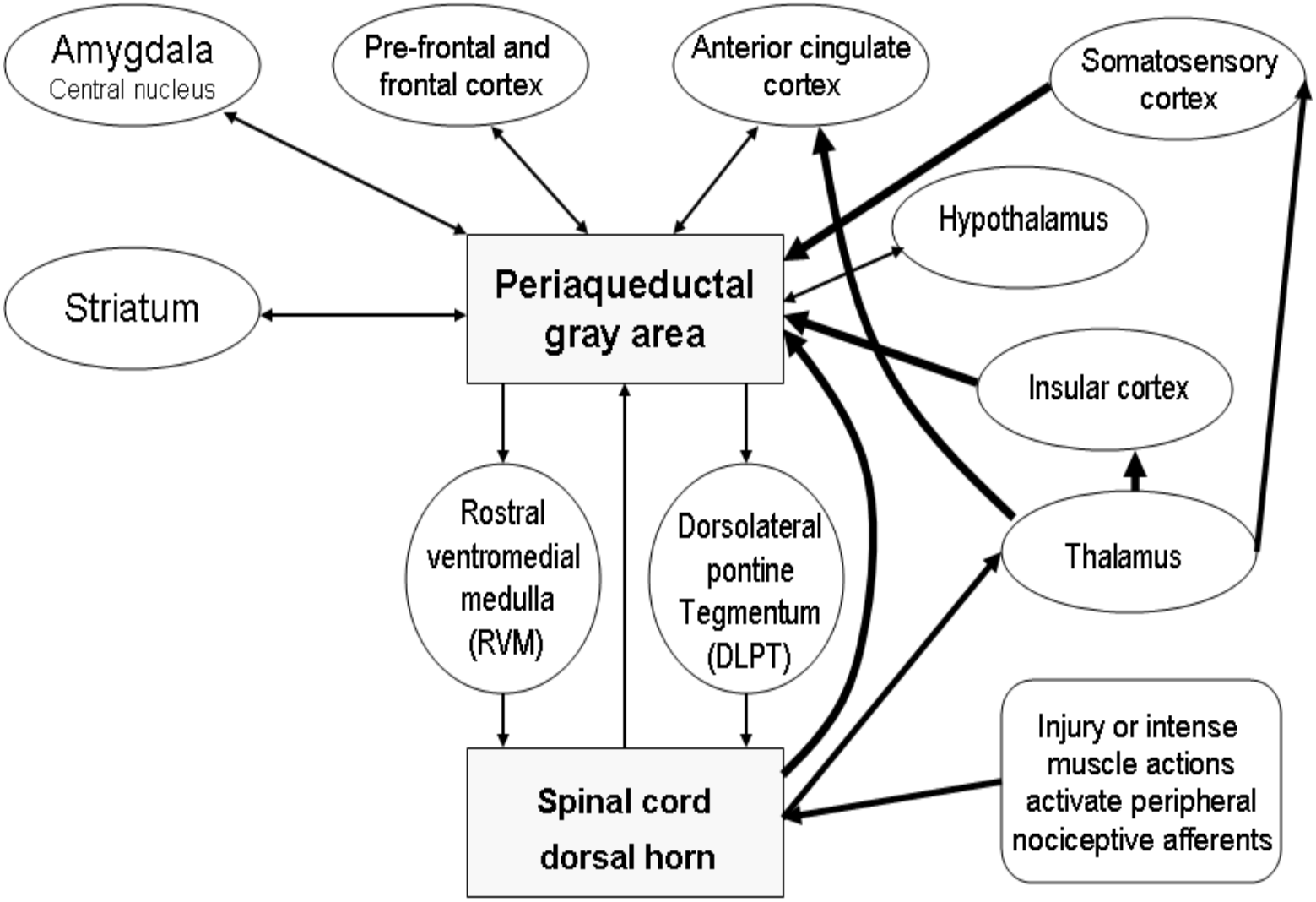
Coherence

- possible, but not definitive



Judging Causal Links

- Biological plausibility
- possible, but not definitive
- conclusion? X / 



Dishman, R. & O'Connor, P. (2009). Lessons in exercise neurobiology: The case of endorphins. *Mental Health & Physical Activity*, 2, 4-9.

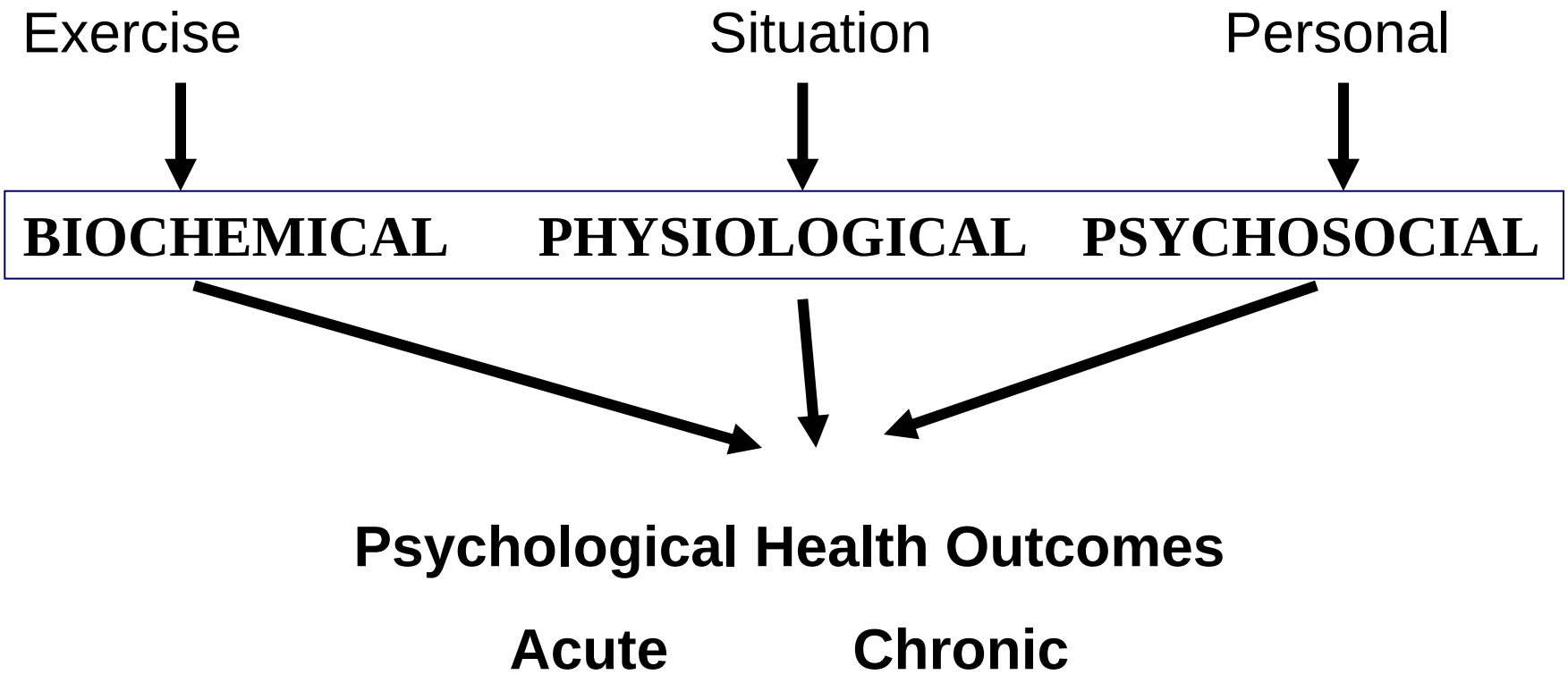
Mental Health

Is influenced by

- genetic inheritance
- childhood experiences
- life events
- individual coping strategies
- social support
- community and environment

DoH (2001)

Effects of exercise



Judging Causal Links

- Biological plausibility
- possible, but not definitive
- conclusion? X / 

- Specificity
- depression is not only affected by exercise
- cannot be supported
- necessary condition?
- conclusion? X

Is the glass half full or half empty?

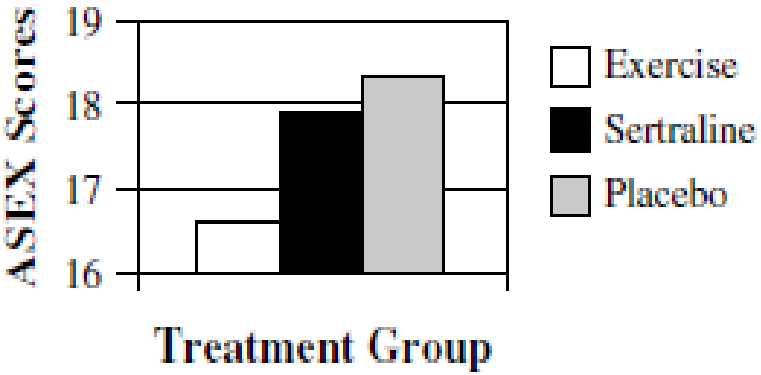
- It might not be causal…it might just be association or even placebo
  - ***the placebo effect is a boon to therapy but the bane of research***

Is the glass half full or half empty?

- We don’t know why it works
  - “We know psychotherapy is effective, but we also know that different apparently contradictory theoretical approaches are approximately equally effective in outcome, but very different in content” (Llewelyn & Hardy, 2001)”

Is the glass half full or half empty?

- it might do harm
  - ***no negative effects reported***
- It might not work
  - ***there are other health benefits: physical activity is 'win-win'***



Hoffman et al. (2009). Effects of aerobic exercise on sexual functioning in depressed adults. *Mental Health and Physical Activity*, 2, 23-28.

Summary

- Physical activity: A ‘win-win’ scenario
- At the population level: physical activity to promote mental health
- At the service level: Assessment & promotion of physical activity should be considered when formulating care plans for mental health service users
- Difficult but not impossible

Richardson, C., Faulkner, G., McDevitt, J., Skrinar, G., Hutchinson, D., & Piette, J. (2005). Integrating physical activity into mental health services for individuals with serious mental illness. *Psychiatric Services,* 56, 324-331. .

Practical Implications: Interdisciplinarity

Primary/Secondary Care

- Developing skills
- Accessing resources in the community
- Legitimizing the role of physical activity?

‘Exercise’ Professionals

- Developing skills
- Developing partnerships and referral opportunities
- Making services accessible