Physiotherapy intervention in Parkinson’s disease: systematic review and meta-analysis

The paper

“Physiotherapy intervention in Parkinson’s disease: systematic review and meta-analysis” by Claire L Tomlinson and colleagues (BMJ 2012; 345: e5004, doi:10.1136/bmj.e5004)

You can read the paper and responses to it by going to student.bmj.com and clicking on the link.

Abstract

Objective—To assess the effectiveness of physiotherapy compared with no intervention in patients with Parkinson’s disease.

Design—Systematic review and meta-analysis of randomised controlled trials.

Data sources—Literature databases, trial registries, journals, abstract books, and conference proceedings, and reference lists, searched up to the end of January 2012.

Review methods—Randomised controlled trials comparing physiotherapy with no intervention in patients with Parkinson’s disease were eligible. Two authors independently abstracted data from each trial. Standard meta-analysis methods were used to assess the effectiveness of physiotherapy compared with no intervention. Tests for heterogeneity were used to assess for differences in treatment effect across different physiotherapy interventions used. Outcome measures were gait, functional mobility and balance, falls, clinician rated impairment and disability measures, patient rated quality of life, adverse events, compliance, and economic analysis outcomes.

Results—39 trials of 1827 participants met the inclusion criteria, of which 29 trials provided data for the meta-analyses. Benefit from physiotherapy was reported for nine of 18 outcomes assessed. Outcomes that might be clinically important were speed (0.04 m/s, 95% confidence interval 0.02 to 0.06, P=0.001), Berg balance scale (3.71 points, 2.30 to 5.11, P=0.001), and scores on the unified Parkinson’s disease rating scale (total score −6.15 points, −8.57 to −3.73, P=0.001; activities of daily living subscore −1.36, −2.41 to −0.30, P=0.01; motor subscore −5.01, −6.30 to −3.72, P=0.001). Indirect comparisons of the different physiotherapy interventions found no evidence that the treatment effect differed across the interventions for any outcomes assessed, apart from motor subscore on the unified Parkinson’s disease rating scale (in which one trial was found to be the cause of the heterogeneity).

Conclusions—Physiotherapy has short term benefits in Parkinson’s disease. A wide range of physiotherapy techniques are used to treat Parkinson’s disease, with little difference in treatment effects. Large, well designed, randomised controlled trials with improved methodology and reporting are needed to assess the efficacy and cost effectiveness of physiotherapy for treating Parkinson’s disease in the longer term.

Why do the study?

Parkinson’s disease is a progressive neurodegenerative disorder that often leads to serious invalidation. Despite advances in neurosurgery and drug treatments, most patients still experience considerable deterioration in physical function. Much research has been conducted to study the possible role of physiotherapy in maximising functional ability. Not all studies showed an effect, and, when present, the magnitude of the effect was different among studies. Additionally, many different types of physiotherapy exist, and it is still not clear which one is the best in Parkinson’s disease.

The authors wanted to summarise the available evidence for the effectiveness of physiotherapy in Parkinson’s disease, to assess its effect size, and to identify the most effective type. They did this by meta-analysis. The sample size of a study is directly proportional to the statistical power—that is, the probability that the study will correctly reject the null hypothesis—the larger the sample size, the higher the power. A meta-analysis combines different randomised controlled trials (RCTs) to increase the overall sample size, thus increasing the statistical power.

Another advantage of meta-analyses is that they allow for more precision in effect sizes, when this differs among studies. A meta-analysis combines the results of multiple studies that test a similar research hypothesis. Therefore, the findings (effect sizes) of individual RCTs are combined using statistical techniques into an overall effect size, sometimes called meta-effect size. The meta-effect size is a more powerful and accurate estimate of the true effect size than in single studies.

What did the authors do?

The authors have conducted a systematic review and meta-analysis of all the available studies on the effectiveness of physiotherapy in Parkinson’s disease. A sound meta-analysis starts with an a priori hypothesis that is, a hypothesis generated before collecting the data. This step is vital to ensuring the validity of the meta-analysis. No matter how tempting it might be to form hypotheses as interesting correlations or patterns seem in the collected data, doing so is likely to bias the meta-analyses irretrievably and diminish its validity. It is analogous to changing the rules of a football game while playing.

The authors should also have written a protocol in which the research question and inclusion and exclusion criteria for the trials to be pooled are clearly described. This study did not have a protocol, but, when looking at the literature search, one gets the impression that this has been very thorough: they searched an extremely large number of biomedical databases for trials dating up to January 2012, and even hand searched a large number of important medical journals. This is an important aspect in systematic reviews and meta-analyses, because as a reader you want to be sure that the authors have done their best to collect all the available relevant research data.

The next step was selection of relevant studies. The authors defined these as “randomised controlled trials (including the first phase of crossover trials) of patients with Parkinson’s disease comparing a physiotherapy intervention with no intervention or placebo control.” Physiotherapy encompasses a wide range of techniques, so they also included trials of general physiotherapy, exercise, treadmill training, cueing, dance, and martial arts versus no intervention. This selection is also an important aspect, as one has to be sure that trials are similar enough to be compared with each other. It would, for instance, make no sense to put a trial on Tai Chi into a meta-analysis with trials on cardiac fitness. In this study the authors excluded all trials that tested multidisciplinary interventions, as they could not tease out the contribution of the separate parts of this therapy.

All articles were read by two independent review authors and data extracted according to predefined criteria, with any discrepancies resolved by discussion. In a meta-analysis it is important that data are extracted by two independent authors, because that limits bias. Two authors is the generally accepted minimum, and one is not regarded as unbiased enough. Once the studies have been selected, it is important to assess their methodological quality, as it would not make sense to mix sound studies with studies of lesser quality. So the authors assessed methodological quality by recording the trials’ eligibility criteria, method of randomisation and blinding, concealment of allocation, similarity of patients in treatment groups at baseline, variation in interventions received by patients throughout the trial period, whether an intention to treat analysis was performed, and the number of patients lost to follow-up.

A meta-analysis always contains a flow diagram depicting the paper selection process, analogous to the patient flow diagram that is obligatory in RCT papers. The authors of this study started with 2595 papers and finally
### Meta-analyses

The authors found that the methodological quality of the included studies was not high—for instance, not many studies described sample size calculation, described randomisation method, or involved blinded assessors.

Meta-analyses are always summarised in so called Forest plots. This paper has many. Figure 2 summarises 19 studies on different forms of physiotherapy, but all with the same outcome measure: walking speed in m/s. Forest plots present the findings for all studies plus (usually) the combined results. This allows the reader to visualise how much uncertainty there is around the results. A central vertical “line of no effect” represents the result if the intervention had no impact. Each included study is shown as a horizontal line with a square in the middle; the location of the square in relation to the central line shows the study’s effect and the length of the line shows the 95% confidence interval. The size of the central square represents the size of the study (or, more precisely, the proportion of the weight that the study contributes to the combined effect).

Here, an increase in speed is seen as a “positive” effect, and therefore studies that showed an increase in speed lie on the right side of the central line. From the figure, we can now conclude that different forms of physiotherapy, and the observed differences in the outcomes that they were measuring, such as gait outcomes, functional mobility, falls, physician-rated disability, and disease specific quality of life.

### What did the study find?

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### What are the strengths and limitations of this study?

A major strength of this review is the effort the authors took in their search: it is unlikely that they missed an important paper on the subject. A limitation is that they did not follow a protocol with an a priori hypothesis. They did use predefined criteria to extract study data.

The obvious limitation of any meta-analysis is that researchers are limited by the available studies. Here, the methodological quality and reporting of the majority of trials was variable, and often inadequate. The trials included in the review were relatively small, and most compared the effect of physiotherapy intervention with no intervention over a short period of time (less than three months). The authors saw no evidence of an improvement in patient rated quality of life after physiotherapy, and the observed differences in the nine significant outcomes were relatively small. Indeed, the differences were so small that one could question the clinical relevance.

### What does this study mean?

The study summarises the evidence base for the effectiveness of physiotherapy for Parkinson’s disease patients. The authors find the general methodological quality of the studies to be low to moderate. The study shows that physiotherapy does improve a number of physical functions, but it is still unclear whether these are clinically significant. It is also unclear whether the effects are sustained on a longer-term basis, and whether some forms of physiotherapy are superior to others.

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**Table 1** Comparison of physiotherapy interventions in relation to speed (m/s). Studies denoted as a or b distinguishes those published by the same first author and in the same year.

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>No Intervention</th>
<th>Weight (%)</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Standard deviation</td>
<td>Total</td>
<td>Mean</td>
</tr>
<tr>
<td>General physiotherapy control</td>
<td>0.13</td>
<td>0.36</td>
<td>24</td>
<td>0.10</td>
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<tr>
<td>Dider 1999</td>
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<td>Ellis 2005</td>
<td>0.16</td>
<td>0.22</td>
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<tr>
<td>Fisher 2006</td>
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<td>10</td>
<td>0.02</td>
</tr>
<tr>
<td>Subtotal</td>
<td>69</td>
<td>83</td>
<td>0.09</td>
<td>0.01</td>
</tr>
<tr>
<td>Subtotal</td>
<td>0.03 (0.01 to 0.01)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise control</td>
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<td>0.15</td>
<td>0.02</td>
<td>0.25</td>
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<td>0.02</td>
<td>0.23</td>
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<tr>
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<td>0.19</td>
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<td>0.17</td>
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<tr>
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<td>0.02</td>
<td>0.27</td>
</tr>
<tr>
<td>Subtotal</td>
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<td>15</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Subtotal</td>
<td>0.03 (0.01 to 0.01)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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