An updated critique of the use of the Twin Spine Study (2009) to determine causation of low back disorder

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Our previous letter to this Journal[1] criticising the "Twin Spine Study"[2] aroused no commentary in your Journal, certainly no contribution supporting the use of the "Twin Spine Study" to deny occupational influences on low back disorder.

Unfortunately this study continues to be quoted by some commentators in the compensation field to "prove" that lumbar spinal disc degeneration arises from genetic factors and such pathology is not influenced even by decades of occupational exposures to recognised risk factors.

As a consequence, coupled with the proposal that radiologically identified deterioration in the structures of the lumbar spine is caused by "degeneration" (ie, a consequence of age alone), Accident Compensation claimants with low back pain are denied cover, subsequent access to treatment modalities and suffer considerable financial hardship as they progress through the long rehabilitation from lumbar disc injury.

We again bring to your readers' attention the errors in this blanket but incorrect application of imperfect epidemiology.

Battié's Twin Spine Study deals with lumbar disc degenerative pathologies primarily based on MRI scan findings (now dated by more modern technology) using a standard but individual protocol, the interpretation of which is radiologist dependent.

This and other twin studies are flawed for this and other reasons.

The initial studies of variance were done in the agriculture domain where multiple identical genetic copies of a plant species could be tested in reasonably tightly controlled environmental conditions. In this case of identical genetic organisms raised in different environmental conditions, the observed differences will be entirely environmental.

In contrast, if one considers organisms of a different genetic make-up (such as lab rats) who are raised in identical environmental conditions, any observed differences will not only be caused by the environment but also can relate to how the individual genes that make up each organism interact with the environment. Thus it is often unclear as to what environmental effect and what genetic features are causing the observed outcome.[3]

Studies in humans cannot be interpreted confidently in either of these situations, and it would be most unlikely that the interaction between the genes and any environmental factors will be a direct linear relationship across all traits and interactions.

Complex conditions, such as many spinal pathologies, will involve numerous genes with different levels of influence. Despite much research, no gene or group of genes has been identified as being responsible for lumbar disc degenerative pathologies.

In order to be valid, these studies also have an unproven "equal environments" assumption, ie, that the environments in which the twins are raised (before occupational exposures) are identical. In addition, these studies have insufficient power to warrant the certainty placed in them.[4]

A 2013 meta-analysis[5] of all studies attributed the hereditability estimate for low back pain (not degeneration) to between 21–67%, a threefold difference.

Eskola et al[6] reviewed 52 genetic association studies in lumbar disc degeneration concluding "*...based on this first extensive systematic review on the topic, the credibility of reported genetic associations is mostly weak. Clear definition of lumbar disc degeneration phenotypes and large population-based cohorts are needed...",* in other words that at this time, there is no identified gene/combination that supports the stated outcomes of the Twin Spine Study.

So while genetics almost certainly plays a role in low back pain (as in most disease states), given the extremely complex interactions between our genes and the environment, assigning a percentage value to an individual based on population data while disregarding personal circumstances is impossible.

As our previous critique of the Twin Study points out, to attribute the predominant cause of lumbar disc injury to genetic factors misunderstands the epidemiology used in this study, confusing *variation* and *causation.*

It is assumed that the percentage of causation adds to 100% for any disease arising from a combination of factors, described in the examples as both genetic and environmental. However, if one again considers the example of Phenylketonuria (PKU),[7] the genetic contribution is 100%, but the disease doesn't exist where the person's diet is phenylalanine free (that is the environmental contribution to causation is also 100%) so that, for example, quoting a >50% contribution (out of 100%) for genetic influences is incorrect.

There are other issues with the structure and assumptions contained within the Twin Spine study and other such studies.

Woszak and Cieslik[8] in a complex review of the validity of assumptions underlying such Twin Studies note the experimental basis of their assumptions and conclusions, and concluded that criticisms of the methodology of these types of studies are "fully justified" and commented *"Consequently, the heritability indices of somatic traits* (for example lumbar disc injury) *should be considered only a provisional measure of genetic polymorphism, expressing an estimated relative contribution of genotypic variance to the phenotypic variance of a given trait"*.

A further critique of the design of such studies is made by Benchek and Morris[9] who comment that the studies rely on untestable assumptions, and these assumptions, if varied, introduce substantial biases.

Again we would point out that there are a myriad of structures in the lower back capable of generating pain, secondary to sophisticated MRI scanning of the lumbar spine we live in the era of "disc injury" although treatment aimed at these disc injuries is often unsuccessful in relieving patient pain.

The recommendations from the Quebec[10] symposium on low back disorder, although dated, are still relevant. This suggests that doctors should diagnose "*low back disorder"* and then comment with varying degrees of certainty about the likely pathology causing this disorder (eg "*L5/S1 disc protrusion; compression fracture L1 vertebral body; of unclear origin"* etc).

Thus the confidence of the authors of and commentators using the Twin Spine study to attribute lumbar disc "degeneration" primarily to genetic inheritance is misplaced.

There are fundamental misunderstandings of the epidemiology as discussed in our previous comment in the *New Zealand Medical Journal*, and Battié's study is based on assumptions that, although superficially attractive, are unproven and subject to inherent inaccuracies that could substantially alter the stated outcomes.

As we have argued in the past, 'degenerative changes' represent a common end pathway to a number of contributing factors,[11] including genetic influences, constitutional (structural) influences, age-related changes and occupational influences, and it would be our proposal that many of the low back 'degenerative' changes identified in working people, in the presence of an history of multiple, 'minor' episodes of low back disorder represent "*post-traumatic osteoarthritis of the lumbar spine*".

Again, the epidemiology of low back pain causation is complex, but in our opinion there is reasonable evidence for an association between specific work factors and low back disorder, best summarised in the dated but still relevant (that is, that has not been superseded) NIOSH epidemiological review.[12]

These factors are supported by a number of more modern studies including the Epilift studies focusing on disc injury that demonstrate a dose response relationship with occupational factors.[13,14] We would argue that the Bradford Hill criteria for this association (Occupational exposure to known risk factors and the development of low back disorder) are reasonably satisfied.

Competing interests:
Nil.

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