Failure to publish trial results exposes patients to risks without providing benefits

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Turin, Italy: Although the publication of results of clinical trials carried out in the USA within 12 months of their completion has been mandatory since 2007, an astoundingly high number of Phase III radiotherapy trials did not do so, according to new research to be presented at the ESTRO 35 conference today (Saturday). An analysis of 802 trials with a primary completion date of before 1 January 2013 showed that 655, or 81.7%, did not publish even a summary result.

Jaime Pérez-Alija and his colleague Pedro Gallego, medical physicists from the radiotherapy and oncology department, Hospital Plató, Barcelona, Spain, also looked at radiotherapy trials that began before the 2007 Act was passed, and found little difference; 422 out of 552, or 76.4%, did not deposit their results with the ClinicalTrials.gov database.

"These findings came as a surprise for many reasons, not least of which was that many of the trials had been funded by the US National Institutes of Health. Since we know that clinical trials produce the best data for decision-making in modern evidenced-based medicine, it is particularly worrying that the law is being ignored on such a wide scale," Mr Pérez-Alija will tell the conference.

One possible reason for non-publication, say the researchers, is that some of the trials may have been granted a deadline extension. But, if this is the case, it is not publicly known. "Therefore, our first problem is that we do not know with any certainty whether a trial is truly overdue. The registry says clearly that all dates must be updated if an extension

has been allowed, but it seems likely that this is not happening in many cases," says Mr Pérez-Alija.

The researchers are investigating the issue further to see, for example, how many of the trials registered in ClinicalTrials.gov or in other databases are being published in medical journals. They will also analyse bias, in the knowledge that it is easier and more usual to publish positive rather than negative findings. They intend to email principal investigators to ask why the mandatory deposition of results did not take place, and to enquire about the reasons for non-publication in medical journals of those trials where there is a published deposition.

"Interestingly, we found that company-funded trials are far better at complying with the rules than academic trials - 55% and 30% respectively. However, only one-third of all the trials we studied were company trials," Mr Pérez-Alija will say.

The researchers broke down their results further by cancer sub-type. The only sub-type where more than half the trial results were published was eye cancer, with 47% unpublished, whereas in testicular and anal cancer the percentage of unpublished trial results was 100% for both categories. Even common cancers such as breast and lung fared badly, with 78% and 73.7% of results unpublished respectively.

"We have shown that a large number of study participants are routinely exposed to the risks of trial participation without the benefits that sharing and publishing results would have for patients in the future. This ethical issue should be at the heart of our current medical practice, and our leaders should be made aware that withholding these data poses a significant threat to public health. Both the US and, more recently, EU laws have made important steps to correct this situation. But if most trials - even those funded by public institutions - do not comply with these requirements, further measures need to be taken," says Mr Pérez-

Alija.

The US Act allows for economic sanctions to be taken against trial sponsors who do not comply with regulations. But the danger here, the researchers say, is that some investigators might decide not to begin a new trial if sanctions are a possibility. Having fewer trials could be damaging to the health system as a whole as well as to future patients.

A potential solution would be to institute a system whereby if clinical investigators apply for public funding, they would have to disclose results of all previously-conducted trials. And for privately-funded trials, results from all previous studies would have to be made available before the new trial could be registered.

"Millions of volunteers have participated in clinical trials to help find out more about the effects of treatments on disease, yet the important ethical issue of reporting results has been ignored widely. Information about what was done, and what was found in these trials could be lost forever, leading to bad treatment decisions, missed opportunities for good medicine, and trials being repeated unnecessarily. This situation should not be allowed to continue," Mr Pérez-Alija will conclude.

ESTRO President Professor Philip Poortmans commented: "Patients who agree to participate in trials do so for the unselfish reason that they want to help others to have the best possible treatment in the future. Not to publish results is unfair to them, to future patients, and to medicine as a whole."

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publish-trial-results-exposes.html