Heavy menstrual bleeding (menorrhagia) is defined as blood loss greater than or equal to 80 ml per menstrual cycle. About 5% of women in the United Kingdom aged 30-49 years seek advice about heavy menstrual bleeding. A systematic review of four studies suggested a prevalence of excessive menstrual bleeding of between 4% and 9%. In the linked systematic review, Middleton and colleagues assess the relative effectiveness of hysterectomy, endometrial destruction, and the levonorgestrel releasing intrauterine system (Mirena) system for the treatment of heavy menstrual bleeding.

First line treatment is generally medical and includes (in order of preference) the levonorgestrel intrauterine system, antifibrinolytic drugs (such as tranexamic acid), non-steroidal anti-inflammatory drugs (such as mefenamic acid and naproxen), progestogens (such as norethisterone and medroxyprogesterone acetate), the combined oral contraceptive pill, and danazol. Except in the case of short course progestogens, these medical treatments are effective in reducing menstrual blood loss.

Surgery may be indicated in women who have completed their family and those in whom medical treatment is futile or intolerable. Hysterectomy (abdominal, vaginal, or laparoscopic) is the definitive surgical treatment. In first or second generation endometrial resection or ablation, the endometrium and underlying basal glands are destroyed. First generation hysteroscopic techniques use an array of electro-surgical or laser tools. Second generation non-hysteroscopic techniques use the controlled application of heat, cold, microwave, or other forms of energy to destroy the endometrium.

Hysterectomy is the only truly effective way to eradicate heavy menstrual bleeding, other treatments manage symptoms alone. However, despite the 100% success rate associated with hysterectomy, it is a major surgical procedure with associated complications, and it has social and economic costs. The rate of serious postoperative complications is about 10%, and long convalescence periods are required. Endometrial destruction techniques have a shorter operation time and hospital stay, quicker recovery, fewer postoperative complications, and comparable rates of satisfaction (70-80%). Women favoured hysterectomy for the outcomes of bleeding and satisfaction (odds ratio 0.04, 95% confidence interval 0.01 to 0.22 at two years; 0.5, 0.3 to 0.8 at two years, respectively). Over time, and even though retreatment may be necessary after endometrial destruction (0.5, 0.3 to 0.8 at two years), some women prefer this less invasive surgical treatment. Retreatment also reduces any economic benefit of conservative surgery over hysterectomy.

Middleton and colleagues found that significantly more women were dissatisfied with the outcome of first generation hysteroscopic techniques than with the outcome of hysterectomy (2.46, 1.54 to 3.93) about one year after surgery. However, hospital stay and time to resumption of normal activities were significantly longer for hysterectomy. Unsatisfactory outcomes were similar with first and second generation techniques, although second generation techniques were quicker and women recovered sooner with fewer procedural complications. Insufficient data were available on the effectiveness of Mirena compared with invasive techniques for any conclusions to be drawn. The review’s findings are in line with other systematic reviews, in spite of the unavailability of at least 35% of the data sought by the review’s authors. As with previous systematic reviews, the inconsistent use of outcome measures in the included studies limits the applicability of the findings.

In terms of clinical practice, the review by Middleton and colleagues supports maintenance of the status quo. Heavy menstrual bleeding is subjective, so the conclusions cannot necessarily be generalised to all women. Quality of life was not significantly better after hysterectomy than with the intrauterine systems, and hysterectomy has serious complications and may not be cost effective. Objective assessment of menstrual fluid loss is essential to determine which women are most likely to benefit from the most radical treatment—hysterectomy. Suggestions include the use of visual analogue scores and pictorial blood loss assessment charts. Most women would be well advised to try a less radical treatment as first line treatment. Research into heavy menstrual bleeding is subjective; the diagnosis is often based on self report, with or without the use of a definitive scoring system for bleeding, and the use of diagnostic criteria is inconsistent.

Comparing surgical versus medical treatments is complex because treatment options (especially medical) are diverse. Further research is needed to compare the more contemporary types of hysterectomy (supracervical, vaginal, and laparoscopically assisted vaginal) with endometrial ablation techniques; and to compare second generation ablation methods with hysterectomy. Trials with at least four years of follow-up are needed for adequate economic comparisons to be made.

Interpreting composite outcomes in trials

Difficulty lies in poor reporting, not the measure itself

The potential problems with the use of composite outcomes in clinical trials are well known. The linked systematic review by Cordoba and colleagues indicates that many of these challenges are long lasting. This review of 40 trials published in 2008 that reported a composite primary outcome found little justification for the choice of outcome, imbalance in the importance of different components in 70% of trials, and problems in the definition and reporting of composite outcomes in 40% of trials. Before we abandon composite outcomes because of the authors’ assertion that their use leads to much confusion and bias, we should consider carefully the opportunity cost and tackle some commonly held misconceptions on composites.

A key advantage of using composite outcomes is that they can increase statistical efficiency and enable us to answer questions that could not otherwise be tackled. Increased efficiency means that trials may be smaller or of shorter duration, allowing effective treatments to be available to patients in a timely manner.

Cordoba and colleagues also question the rationale for the choice of components of the composite. Consistency in the use of composites for a particular disease undoubtedly aids interpretation. Thus, in the development of new treatments in heart failure and subsequently in cardiovascular disease more generally, the composite outcome of unplanned hospital admission for cardiovascular reasons and all cause mortality has become the standard primary outcome for regulatory trials. Consensus on appropriate composites could be adopted in other clinical areas.

The concern that composite outcomes can lead to the incorrect perception that end points such as mortality are reduced by treatments that only show significant benefits on other less important components is also not new, and the Food and Drug Administration (FDA) in the United States seems to have dealt with this. The ATHENA trial, which recently examined the effects of dronedarone in elderly people with atrial fibrillation and additional risk factors for death, adopted the primary outcome of all cause mortality and unplanned hospital admission for cardiovascular disease. Although dronedarone had a strong effect on the composite and on the hospital admission component, its effect on all cause mortality alone was not significant. The FDA duly excluded mortality from the indication (which governs marketing activity for the product), stating that dronedarone had been shown to “reduce the risk of cardiovascular hospitalisations.” Furthermore, although a secondary outcome of death from cardiovascular disease was significant, this was not included in the US indication, presumably because the two components of the composite primary outcome were considered first in the alpha spending approach, which preserves the study-wide type 1 error of 2.5% for benefit. In other words, the trial was deemed to have used up all its available statistical information to answer questions before reaching the apparently nominally significant outcome of death from cardiovascular disease.

So if the regulators, at least in the US, have raised their game, why then are journals still doing such a poor job? Some may feel that Cordoba and colleagues are making too much of the data they present: 87% of primary composite outcomes they assessed were presented consistently in papers, although the wording was ambiguous in 20% 78% provided data for the components of the composites.

Cherry picking in outcome measures is not restricted to the components of composite outcomes and is always wrong. Journals should examine the original trial protocols and ensure that outcomes are reported fully, accurately, and honestly. They should also ensure that data on each component of a composite are reported, even when a composite has many components (such a table could be included as additional web based material if too large to be included in the standard publication). This not only helps interpretation but ensures that data from trials with composite outcomes can be included in meta-analyses.

Cordoba and colleagues advance the idea that all components of a composite outcome should be similarly important. Although superficially attractive, this premise can be challenged. Packer has argued that mortality is not the only adverse clinical event worth considering in a clinical trial, and it is an incomplete measure of disease progression. He makes the point that many patients with heart failure deteriorate symptomatically, are repeatedly admitted to hospital for worsening symptoms, and require intensive therapeutic interventions yet they are still alive at the end of the study. If the primary outcome measure is all cause mortality, “such patients would be considered (inappropriately) to have fared as well as patients who remained clinically stable and minimally symptomatic.”

It is a common misconception that the primary outcome in a clinical trial should be the most important outcome. Instead, the primary outcome “should be the variable capable of providing the most clinically relevant and convincing evidence directly related to the primary objective of the trial.” For example, it would be wrong to have all cause mortality as the primary outcome of a trial that would have insufficient statistical power to provide a reliable answer on that outcome. Thus the end point must be important, but not necessarily the most important, and must take into account estimation issues such as the number of available patients and predicted event rates; too few patients or events may preclude the examination of some rarer end points in a
In trials of heart failure, investigators have increasingly included only important hospital admissions (such as those that are unplanned, involve an overnight stay, and are for cardiovascular reasons) to avoid including relatively unimportant events.7

Composite outcomes attract surprisingly violent reactions from some authors.8-11 But we do not argue that randomised trials should be abandoned because investigators sometimes cherry pick the results.8 We should proscribe cherry picking rather than composites. As Cordoba and colleagues have pointed out, composite outcomes are sometimes poorly reported in journals. We have the collective opportunity to correct this limitation and raise our game in the same way that the FDA has done. If we are to benefit from the potential advantages of composite outcomes, we must not be frightened by the hard work that this opportunity affords us.

5. Freemantle N. Interpreting the results of secondary end points and subgroup analyses in clinical trials: should we lock the crazy aunt in the attic? BMJ 2001;322:989.

Access to welfare benefits in primary care

Is not substantially linked to GP patterns of certification behaviour

In the linked study, Whittaker and colleagues assess variations in primary care patients who claim incapacity benefit, and whether consultation behaviour in primary care can be used to predict those people with mental health problems who are more at risk of becoming dependent on state benefits for long term health problems.1

Internationally the pressure to reduce the proportion of people of working age who depend on state benefits and other benefits is increasing. Recent reviews in the United Kingdom have reported the scale of the problem and associated costs; they have proposed a variety of reforms, some of which, such as the introduction of the new Med 3 certificate (the “fit note”) in April 2010, have already had an effect on sickness certification processes for general practitioners.2 In the UK, the cost of mental ill health in terms of sickness absence, associated benefits, and lost productivity is substantial, and that of absenteeism and presenteeism (being in work when relatively unfit) exceeds the NHS annual budget.2 4 Recent guidance from the National Institute for Health and Clinical Excellence (NICE) confirms the lack of robust research to guide practice and government initiatives.5

A recent study of trends in incapacity benefit shows a wide variation in rates across the UK and suggests that the 4% fall in the total number of people on this benefit between 2000 and 2008 reflects fewer new claimants (rather than more claimants moving back into work, claiming jobseeker’s allowance, or retiring (outflow)).6 Another study reported a steady rise in the proportion of claimants with a mental illness, and an association between mental illness and previous unemployment.7 This mirrors the finding that mild to moderate mental health diagnoses are predominant (43% of total days) in sickness certificates and are risk factors for prolonged absence and subsequent incapacity.8

Being out of work is bad for health, and increasing evidence shows that good work (which reflects elements of fair pay and conditions, job control, and satisfaction) is good for health.2 In times of increasing financial pressures and falling employment policy makers attempt to maximise access to good work and reduce the costs and consequences of not having work. Many factors influence the path to work or incapacity, such as work opportunities (range of job vacancies available), support for disabled workers, work (“bad” work) related ill health, the welfare structure and payments system, socioeconomic environments, and cultural expectations. Participants within these structures include the claimants, managers and human resources, practitioners who moderate sickness absence (occupational health, general practitioners, and specialists), and policy makers.

Whittaker and colleagues looked for risk factors related to incapacity benefit claims by analysing data from the Scottish

Statement of Fitness for Work

For social security or statutory sick pay

Patient’s name
Mr, Ms, Mrs, Ms, Ah

I assessed your case on
and, because of the following condition(s):

I advise you that:

[ ] you are fit for work.
[ ] you may be fit for work taking account of the following advice:

[ ] phased return to work
[ ] amended duties
[ ] reduced hours
[ ] workplace adaptations

Comments, including functional effects of your condition(s):

If available, and with your employer’s agreement, you may benefit from:

[ ] phased return to work
[ ] amended duties
[ ] reduced hours
[ ] workplace adaptations

Cite this as: BMJ 2010;341:c3642 doi:10.1136/bmj.c3642
Imagine a vibrant field of scientific inquiry. Researchers focus on solving the most urgent uncertainties of the discipline and publish papers that, guided by reporting guidelines and further improved by pre-publication peer review, provide comprehensive accounts of their methods, findings, and limitations. The research community, keen to advance the field, engages in an active dialogue regarding the validity and implications of each new paper. Post-publication critique, as the final arbiter of the meaning of each new communication, is no less important than the earlier phases and is a sign of a healthy scientific community, a community actively working to determine the validity and importance of a paper, the current suboptimal post-publication review process. Because peer review is imperfect, and evidence shows that most published papers have important flaws in methods or reporting, the first explanation—that papers are of such high quality that no critique is needed—can be quickly dismissed.

Interventions to reduce absenteeism and incapacity claims for those in employment focus on preventing sickness absence or facilitating return to work through role and workplace modification, occupational health support, case worker support, targeted timely interventions, and negotiations for shorter absence. Evaluations of these interventions must be robust enough to explore the potential for harm as well as benefit, because going to work when not fully fit can harm the person concerned, his or her contacts, and employers. This new research is a welcome addition to the existing sparse evidence base. To improve access to welfare for those in need and to support those at risk of drifting into long term unemployment, we need more investment in research that can inform policy and help translate the findings into practical solutions.

Inadequate post-publication review of medical research
A sign of an unhealthy research environment in clinical medicine

Imagine a vibrant field of scientific inquiry. Researchers focus on solving the most urgent uncertainties of the discipline and publish papers that, guided by reporting guidelines and further improved by pre-publication peer review, provide comprehensive accounts of their methods, findings, and limitations. The research community, keen to advance the field, engages in an active dialogue regarding the validity and implications of each new paper. Post-publication critique, as the final arbiter of the meaning of each new communication, is no less important than the earlier phases and is a sign of a healthy scientific community, a community actively working to move the field forward.7,4

In the linked study, Gøtzsche and colleagues’ finding that authors of BMJ articles are reluctant to respond to criticisms submitted as rapid responses reinforces the finding of the few previous studies, which found consistent evidence that all aspects of post-publication review are wanting in medical research. Most research articles in medical journals receive no critique, and, for the minority that do, authors often do not reply or reply but do not respond to the criticism. Instead of illuminating the factors that would help the community determine the validity and importance of a paper, the current post-publication review process typically leaves key concerns unresolved.

Given that science is fallible, what should we conclude about a field of scientific inquiry where post-publication review is lacking? Is the problem with the post-publication peer review process, the prevailing culture, or the publications themselves? The table lists factors that could contribute to a suboptimal post-publication review process. Because peer review is imperfect, and evidence shows that most published papers have important flaws in methods or reporting, the first explanation—that papers are of such high quality that no commentary is needed—can be quickly dismissed.

We can only speculate about the extent to which the low volume of letters is a function of the papers (which are often
Reasons for the absence of adequate post-publication peer review

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<tr>
<th>Reason</th>
<th>Causes</th>
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<td>Paper perfect</td>
<td>No criticism needed (rare occurrence since few papers are perfect and all papers need to be placed in context of previous work)</td>
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<tr>
<td>Paper imperfect yet no feedback submitted</td>
<td>Paper trivial, unworthly of comment</td>
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<td></td>
<td>No one reads the paper</td>
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<td></td>
<td>Readers fail to detect flaws</td>
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<td></td>
<td>Readers assume that prepublication peer review has eliminated important errors</td>
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<td></td>
<td>Readers uncomfortable or scared to publicise flaws</td>
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<td></td>
<td>Readers dissuaded by logistics (eg, due date, word limit)</td>
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<td>Reader notices flaw after deadline passed</td>
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<td></td>
<td>No reward for writing a letter</td>
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<td>Reader believes letter unlikely to be published</td>
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<td>Reader believes letter unlikely to have any effect</td>
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<tr>
<td>Feedback submitted but not published</td>
<td>Journal conflict of interest</td>
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<td></td>
<td>Unreasonable constraints (eg, no more than 3 letters about each paper, letter arrives too late)</td>
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<td>No published response from authors</td>
<td>Authors' egos or motivations</td>
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<tr>
<td></td>
<td>No disincentive for non-response</td>
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<tr>
<td>Author response inadequate</td>
<td>Evasive responses are common and accepted by journals</td>
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<tr>
<td>Failure to resolve outstanding issues</td>
<td>Second set of correspondence extremely rare</td>
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written to promote the authors or a product rather than move science forward and benefit patients), the readers (errors are not detected or readers who see them don’t bother writing), or the editors (who resist publishing critical letters that impugn their article selection and review process). Today’s research contributes to tomorrow’s systematic reviews, so an important flaw in a publication should be highlighted whenever identified. It is therefore regrettable that journals discourage letters through needless constraints on length, the allowed time window, the number of letters they will publish, and their refusal to publish several rounds of letters,11 12

Journals have been exercised about competing interests of authors and reviewers. Yet journals have a strong conflict of interest regarding letters to the editor because publishing criticisms of journal articles suggests that the editors are not doing their job and may lower the prestige of the journal, and handling correspondence requires journal resources. There is a case for an independent letters editor.

If logistics were the sole problem we would expect that web based rapid response features that remove many of the logistical difficulties of publishing a critique would be popular. They are not widely used by (largely) paper based journals other than the BMJ,7 and when they are used, they often fail to get complete responses from the paper’s authors, which suggests that logistics are not the sole cause of inadequate post-publication review.

The inadequacy of authors’ responses to criticism suggests that authors feel no obligation to respond to reasoned criticism, and letter writers may fear that they will be perceived as picky or anti-collegial for pointing out flaws. Such a culture impedes the progress of science by stifling the open communication that makes the literature self correcting and is essential to the scientific process.7

Finally, the volume and quality of scientific papers may contribute to the problem—a mountain of poor quality unfocused literature has left its readership fatigued, numb, and passive. Each year more papers are published than the year before (about 500 000 research papers were added to Medline in 2009), but the number of letters stays the same. Each new paper is another monologue added to the heap. Few read it and fewer care. Errors remain unnoticed or unnoted, and no one seems terribly bothered.

The solution to the absence of effective post-publication reviews does not lie within its mechanisms; it requires a fundamental reworking of what research is performed, how it is presented, and how it is assimilated into current knowledge. We need fewer papers that are of higher quality and importance. We also need a change in culture to value public discussion if we are to re-engage the medical research community in the kind of post-publication review process that patients deserve."9

5 Gøtzsche PC, Delamothe T, Godlee F, Lurndh A. Adequacy of authors’ replies to criticism raised in electronic letters to the editor: cohort study. BMJ 2010;341:c3926.

Listen to Peter Gøtzsche and Tony Delamothe discuss the implications of this research at www.bmj.com/podcasts

Open access publication fees at the BMJ

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EDITORIALS

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Competing interests: FG and TG are editors of the BMJ. They will not, however, benefit directly from this new policy.
Provenance and peer review: Commissioned; not externally peer reviewed.
Please see http://resources.bmj.com/bmj/about-bmj/about-bmj/policies/open-access-policy for further information on author fees at the BMJ and frequently asked questions (FAQs).

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We neither wish nor intend to deter anyone from submitting research to the BMJ. We appreciate that research—even in high income countries—is often unfunded or may be supported by a patchwork of different resources, and that even those funders who support open access will not always cover extra costs arising downstream from a primary study. So the options for all research authors will be either to pay the fee or not to pay it: the BMJ will not have a sliding scale of fees. Nor will we seek a fee for publishing other types of article, such as editorials, clinical reviews, analysis articles, or research methods and reporting articles.

We are introducing this policy as the next step in our efforts to ensure the sustainability of open access publication of research in the BMJ, and we are doing so in the spirit of experimentation. Many research funding organisations, sponsors, and universities now provide grants that cover journals’ fees for open access publication, and most other open access journals levy such fees to cover the costs of peer review, journal production, and online hosting and archiving. Because the BMJ is providing open access to research and funders are providing fees, it makes good sense for the journal to defray at least some of its publishing costs in this way.

The BMJ was one of the first scientific journals to make the full text of its articles freely available online, starting in 1998. From very early on our policy included immediate deposition of the full text in the National Library of Medicine’s archive PubMed Central, as well as allowing authors to retain copyright and to share and reuse (non-commercially) their articles. Although research has remained freely available to everyone, from 2005 access controls were gradually introduced for non-research content (although the whole journal remains freely accessible to institutions in 113 low and low-middle income countries through the BMJ Group’s membership of the HINARI initiative (http://group.bmj.com/products/journals/countries-with-free-access).1

Access controls were introduced to maintain subscription revenue as a contribution to the costs of commissioning, peer reviewing, editing, and publishing the BMJ’s editorials, education, comment, features, and news. Using subscriptions to non-research content to subsidise access to research distinguished the BMJ from the other open access journals that sprang up subsequently. Yet the BMJ was not formally recognised and listed as an open access journal until October 2008 (http://resources.bmj.com/bmj/about-bmj/policies/press-release-greater-openness-the-future2014-the-bmj-and-open-access). Now the BMJ has a full set of open access credentials: a Creative Commons licence (http://resources.bmj.com/bmj/authors/editorial-policies/copyright), membership of the Open Access Scholarly Publishers Association, and—as from now in a limited way—authors’ fees.

Some publishers with an open access option have promised to titrate journal subscription rates and site licences for institutions’ against revenue from authors’ fees, once that income exceeds a certain threshold. The BMJ has no plans to do this, for several reasons. Firstly, our foray into charging authors’ fees is an experiment, and we aim to evaluate its success before going any further. Secondly, we do not expect authors’ fees for BMJ research articles to come close to covering the costs of peer review for submitted research, given that we publish around 300 research articles a year but receive more than 4000, and given that only a minority of published research is likely to come with open access funding. Thirdly, we aim to increase the amount of non-research content we publish, in response to reader feedback requesting more education, comment, and news alongside the BMJ’s peer reviewed research. Author fees cannot and should not be expected to cover the costs of creating this extensive and growing range of clinical and journalistic material, which will continue to be funded through subscriptions and advertising (http://resources.bmj.com/bmj/about-bmj).

Last but definitely not least, we are pleased to introduce a new sister journal to be launched this autumn, BMJ Open (www.bmjopen.bmj.com). This is an online open access journal that will provide rapid publication of research across all medical disciplines and therapeutic areas, and which will welcome both high and lower impact studies to ensure that well conducted studies find a home where they can be fully reported. We particularly hope that BMJ Open will attract work that deserves publication but does not quite meet the specific needs of the audiences of the BMJ and the BMJ Group’s specialist journals. All authors whose work is accepted by BMJ Open will be asked to pay an article processing charge. Fees will be waived for authors without the means to pay, and as with the BMJ, editors will be unaware of the payment status of articles when they are making their decisions on publication. All articles will be openly peer reviewed and, if accepted, will be published with reviewers’ comments and other background information. As well as publishing full research reports in the traditional way, BMJ Open will encourage transparency at all stages of the research dissemination process by publishing study protocols, pilot studies, and pre-protocols and by facilitating the sharing of raw data either as additional electronic material or through direct links to data repositories.

With the introduction of author fees for some of the open access research published in the BMJ, and with the launch of our new online journal BMJ Open, the BMJ Group continues its support for both open peer review and open access to peer reviewed research. We hope you will join us by sending us your work.


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