

### Is it ethical to use drosiprenone-containing combined oral contraceptives?: authors' response

Dr Pittrof's response<sup>1</sup> to our review of recent studies on the association of oral contraceptive use and the risk of venous thromboembolism (VTE)<sup>2</sup> discusses the ethical implications of the study results on clinical decision making. His arguments are based on four principles of bioethics, as outlined in the sixth edition of Beauchamp and Childress' landmark textbook on biomedical ethics.<sup>3</sup>

One of us (JD) remembers with great pleasure Beauchamp's and Childress' lectures at the Kennedy Institute of Ethics at Georgetown University. Their undogmatic and brilliant intellectual contributions have influenced several generations of bioethicists since the late 1970s. Their approach to the establishment of principles that provide general normative frameworks in bioethics ("principlism") has been criticised since the late 1980s, when several different methods and types of moral philosophy began to be proposed as alternatives or substitutes (such as Impartial Rule Theory, Casuistry and Virtue Ethics). However, these new approaches are, in fact, not inconsistent

with an undogmatic and broad interpretation of a principle-based account.<sup>4</sup>

Therefore, in Pittrof's arguments the starting point seems to be justifiable, with the proviso that some oversimplifications of theoretical ethical conflicts of considerable complexity are perhaps attributable to the limited space available in a letter to the editor. His conclusion that respect for patients' autonomy implies the obligation of physicians to provide sufficient information for her to form her own opinion is both correct, as well as challenging. Clinical experience and empirical data indicate that patients exhibit wide variation in their understanding of information, and debate continues about the level of understanding that is essential for valid consent (see Beauchamp and Childress, p. 127).<sup>3</sup>

Nevertheless, some of Pittrof's arguments cannot remain unchallenged. Our review addressed only studies of VTE and, as is obvious, the risk/benefit assessment of drosiprenone (DRSP), a hormone with progestogenic, anti-androgenic and aldosterone-antagonistic properties, cannot be based solely on a single adverse clinical outcome. Hence, based on our review, the two basic principles of biomedical ethics that have enjoyed a remarkable degree of continuity over the past two and a half millennia, non-maleficence ("do no harm") and beneficence ("do good") cannot be judged. Given the existing evidence on arterial thromboembolism<sup>5</sup> and the effectiveness of the 24-day regimen of DRSP<sup>6</sup> we agree with Pittrof that "DRSP-containing COCs are better for some patients than other COCs" – although our estimate of the absolute number of patients potentially benefiting from its use would probably be higher than his.

The most recent report on the risk of VTE among hormonal contraceptive users was commissioned by the US Food and Drug Administration (FDA), and published on its website.<sup>7</sup> As yet, however, it has not been published in a peer-reviewed journal – and until it has been, its validity cannot be judged. But setting that matter aside, it is unclear why, according to Pittrof, the 15 to 11 vote of the FDA Advisory Committee that the benefits outweigh the risk of DRSP-containing combined oral contraceptives (COCs) "activates" the non-maleficence principle. In any risk/benefit assessment it is always necessary to balance potential benefits against potential harmful effects, and non-maleficence and beneficence need to be considered without any inherent hierarchical ordering (see Beauchamp and Childress, p. 151).<sup>3</sup> There is no indication that the Advisory Committee members' assessment did

not follow these fundamental ethical principles.

Pittrof's definition of 'justice' ("achieving the highest level of health given the available resources") is actually based on a utilitarian concept of distributive justice and ignores, for example, the libertarian approach (see Beauchamp and Childress, pp. 244–248).<sup>3</sup> Furthermore, in the vast majority of countries DRSP-containing COC prescriptions either are not reimbursed, or are only partially reimbursed. In addition, in the UK the 24-day regimen is not available to women receiving medical care under the National Health Service and the 21-day regimen is often restricted in local formularies. If a medication is not reimbursed then Pittrof's definition does not apply, and if its use is restricted to specific clinical situations in which patients benefit from its use, 'justice' is not an issue.

In our review we concentrated on methodological issues in observational research, not on ethical considerations. Furthermore, we did not assess the overall risk/benefit associated with DRSP-containing or other progestogen-containing COCs. But to repeat, according to our assessment the best evidence continues to suggest that among COCs with the same dose of ethinylestradiol, the risk of VTE is a class effect. Based on a careful risk/benefit assessment, and on the considerations given above, we do not believe that prescribing a DRSP-containing COC poses an ethical issue.

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**Competing interests** Jürgen Dinger was previously an employee of Schering until 2004. He presently conducts, and in the past has conducted, studies which are/were supported by research grants from manufacturers of contraceptives. Samuel Shapiro presently consults, and in the past has consulted, with manufacturers of products discussed in this article.

*J Fam Plann Reprod Health Care* 2012;**38**:206–207.  
doi:10.1136/fprhc-2012-100381

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