MIDTERM ASSIGNMENT IN MFEL3010

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The two papers evaluate the same phenomenon, but reach two radically different conclusions. My assignment in this essay is to evaluate why.

Colorectal cancer (CRC) develops from normal colonic mucosa that undergoes transition at the genetic level and leads to growth of adenomatous lesions[1]. The occurrence of adenomas increases proportionally to the age[2]. For gastrointestinal diseases like these, endoscopy is the most important tool for screening and ablation. But this instrument could lead to life-threatening complications (something also a possible surgery could)[3].

In the study by Holme et al. the investigators point out that screening reduced CRC incidence by 20% and CRC mortality by 27%. They also compared their findings to three other comparable studies that made similar conclusions[4]. Each adenoma detected and referred to an examination reduces the mortality. They also conclude that screening is as important for age groups below the traditional 55-64 and that screening is more important for men based on the statistics[5].

Prasad et al.'s point of view is starkly different. This study group's opinion, based on statistics, is that too much emphasis is placed on the mortality of specific diseases rather than total mortality[6]. They show that despite the decrease in the diseases that were screened (like CRC), the overall mortality was unchanged. An important part of their argument is that over-diagnosing and overtreatment compensates for the number of deaths, due to factors as

[1] Hagland et al. *Molecular pathways and cellular metabolism in colorectal cancer*: 2013 : 12
[2] Ibid : 14
[3] Kwan V. *Advances in gastrointestinal endoscopy.* 2012: 118-119
[4] Holme et al. *Effect of flexible sigmoidoscopy screening on CRC incidence and mortality: A randomized clinical trial.* 2014 : 7
[5] Ibid : 8
[6] V. Prasad et al. *Why cancer screening has never been shown to "save lives" – and what we can do about it.* 2016 : 1

complications that follow overtreatment. The phenomena called false positive (meaning given a diagnosis when healthy) leads to further harm like for example psychological issues[7].

Normally an objection to a medical point proven would be to emphasize on the weakness of the clinical trials (like lack of duration, number of patients and likewise), but Holme et al. reflect on these aspects just fine. Referring to three other papers further advances their case. But they do not address the incoherence regarding the surrogate end points and real end points. It is worth considering if screening represents the surrogate point while total mortality (over-diagnosing) is the real end point.

The last point to consider is the compliance-factor. Holme et al. suggest that in case of full compliance the absolute reduction in CRC-risk would be twice as high. Also worth mentioning that CRC incidence rate for non-compliers was the same as for control group[8]. This implies that under such conditions the effect of the screening would be much stronger, but would it negate Prasad et al.'s point? Not necessarily since Prasad et al. explain that the number of false positive results is much larger than assumed (for example 60% in one mammography-trial)[9].

Probably would a convergence in method between these two sets of opinions be the best future ahead for screening. A disease-specific screening that attaches importance to overall mortality and the problems with over-diagnosis would be such a convergence.

[7] Ibid : 8
[8] Holme : 9
[9] Prasad : 3

Literature:

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