

# Disparities in the Incidence and Outcome of Endometrial Cancer: Interviews with Two Key Opinion Leaders



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## Interview Summary

Endometrial cancer is a common gynaecological cancer in high-income countries, and is often associated with comorbidities. The incidence and mortality of endometrial cancer are increasing globally. Disparities in the incidence and outcome of gynaecological cancers are complex and multifactorial. Disparities in patient management and outcomes among patients with endometrial cancer arise from racial, socioeconomic, educational, and geographical barriers that influence

treatment and survival. Differences in access to treatment and adherence to treatment guidelines, including inequalities in surgical care, adjuvant chemotherapy, and radiation treatment, have been shown in numerous studies in the USA, but there are few treatment disparities in Europe, where therapy is easier to access for all populations. Biological factors, such as comorbidity, are an important cause of disparity among females with endometrial cancer across the globe. For this article, EMJ conducted an interview in October 2023 with two key opinion leaders: Mansoor Raza Mirza from Rigshospitalet, Copenhagen University Hospital, Denmark; and Isabelle Ray-Coquard from Centre Léon Bérard, Lyon, France, both of whom have a wealth of experience and expertise in the clinical management of endometrial cancer, and have conducted many research projects in this area. The experts gave valuable insights into topics such as racial and socioeconomic disparities in patients with endometrial cancer; the importance of comorbidities, such as diabetes, hypertension, and obesity; and the impact of lifestyle on the development and outcome of this disease. Mirza and Ray-Coquard also discussed treatment disparities and inequity, covering topics including access to treatment and adherence to treatment guidelines. Finally, the experts described how healthcare disparity and inequity in the management of patients with endometrial cancer might be addressed in the future, and the changes they would like to see.

## INTRODUCTION

Endometrial cancer is one of the most common gynaecological cancers in high-income countries,<sup>1</sup> and often presents with comorbidities.<sup>2</sup> In contrast to many other cancer types, the incidence and mortality of endometrial cancer are increasing,<sup>3-5</sup> at least in part because of the global obesity epidemic.<sup>3</sup> Disparities in the incidence and outcome of gynaecological cancers are complex and involve biological factors, as well as racial, socioeconomic, and geographical barriers that influence treatment and survival.<sup>6</sup> For example, striking differences have been reported between early-onset endometrial cancer (age at diagnosis <50 years), which is relatively uncommon, and late-onset endometrial cancer (age at diagnosis ≥50 years) in terms of demographic and tumour characteristics, as well as racial and ethnic patterns, and time trends in endometrial cancer incidence.<sup>5</sup> The faster increases in early-onset compared with late-onset endometrial cancer incidence rates, particularly among non-White females, are similar to that observed in other cancers, and indicate a possible link with the rising obesity epidemic in younger generations.<sup>5</sup> Ling et al.<sup>7</sup> reported that, in contrast to the declines in all-cause mortality rates at all ages, cancer-related mortality has increased in older individuals with Type 2 diabetes, particularly for colorectal, pancreatic, liver, and endometrial cancers. They suggested that tailored cancer prevention and early detection strategies are

needed to address persistent inequalities in the older population, the most deprived, and smokers.<sup>7</sup> Healthcare disparities and inequity in endometrial cancer are gaining increasing interest in the oncology community as part of the continuous drive to improve patient outcomes.

## RACIAL DISPARITIES IN OUTCOMES FOR PATIENTS WITH ENDOMETRIAL CANCER

Mirza and Ray-Coquard explained that research into racial disparities in endometrial cancer is primarily conducted in the USA. The research indicates that Black females with endometrial cancer have a higher readmission risk following surgical management of disease,<sup>8</sup> poorer prognosis,<sup>9</sup> and higher mortality rates<sup>10-12</sup> compared with White females with this disease, even in equal-access healthcare populations.<sup>13,14</sup> Reported differences that could account for the worse survival of Black patients with endometrial cancer include more aggressive histopathologies (such as serous carcinoma<sup>15</sup> and carcinosarcoma),<sup>16</sup> and molecular alterations,<sup>14,17-19</sup> including upregulation of molecules driving cell cycle progression, as well as p53 and human epidermal growth factor receptor 2/neu signalling.<sup>17</sup> Other factors across the spectrum of care that may influence the survival disparities between Black and White patients include timely access to guideline-concordant care, clinical trial enrolment, and systemic racism.<sup>20</sup> In

addition, Black patients with endometrial cancer are reported to be less likely to express cancer distress, which has been associated with worse clinical outcomes, and to have fewer referrals for support services compared with White patients with this disease.<sup>21,22</sup> Country of birth has been shown to influence endometrial cancer overall survival in disaggregated subpopulations of Black females.<sup>23</sup> Furthermore, heterogeneity in endometrial cancer incidence and survival patterns has been reported among different Black populations in the USA.<sup>24</sup> These findings indicate an interplay between genetic and socioenvironmental factors.<sup>24</sup> Although these disparities in endometrial cancer outcomes according to race are well documented, intervention work to address the mortality gap is limited.<sup>25</sup>

Although study data from the USA show a clear racial disparity in outcomes and survival of patients with endometrial cancer, Ray-Coquard noted that the recording of patient demographics in clinical studies in some European countries differs to that in the USA. In France, where Ray-Coquard is based, the law prohibits the recording of a clinical study subject's race in their case report form. Therefore, the impact of race on the efficacy and safety of treatments or interventions investigated in the clinical study, and any race-associated disparities, cannot be determined. Mirza stated: "We must influence politicians and ethics committees to reconsider the collection of clinical study data on race in countries where it is currently prohibited. These data are extremely important, particularly in countries such as France, where there are large populations from Northern Africa, to establish how well different patient populations are responding to treatment, and to enable any racial disparity in European-based populations to be identified." Ray-Coquard added: "If we do not collect the data on race, we are not able to answer the question about the impact of race on outcomes."

Even though there is no such law prohibiting the recording of race in case report forms in Denmark, where Mirza is located, there are limitations to recruitment in this country that impact study population diversity in clinical trials. For example, Mirza disclosed that recruiting patients from Greenland (a territory of Denmark) into clinical trials in Denmark is not feasible because of language differences

(Greenlandic versus Danish), and the difficulty of follow-up when patients return to Greenland. The Greenlandic government permits patients from Greenland to attend Danish hospitals for treatment, but does not allow them to stay in Denmark longer than would be required for the standard of care treatment. Therefore, patients from Greenland entering a clinical trial in Denmark would be required to travel often between the two countries. This travel would be at a cost to the Greenlandic government, which is not sustainable, and precludes inclusion of these patients in the clinical studies.

Restrictive eligibility criteria for clinical trials often result in the exclusion of certain patient populations, which adds to the widening disparities seen between patients who enrol in trials and those treated in routine practice.<sup>26</sup> Even if restrictive eligibility criteria are not in place, Mirza acknowledged that very few Black and Asian females are included in the endometrial cancer clinical trials in which he is involved, and suggested that there needs to be more effort to ensure these populations are well represented in clinical research. Mirza observed that non-White females are eager to participate in clinical trials, so this is not a limiting factor, but there is a 'shockingly low' percentage of this population in global trials.

## **SOCIOECONOMIC DISPARITIES IN PATIENTS WITH ENDOMETRIAL CANCER**

Area-based socioeconomic deprivation has been established as an important indicator of health, and a potential predictor of survival in patients with endometrial cancer.<sup>27</sup> According to Luo et al.,<sup>28</sup> gaps in access to appropriate cancer care in the USA, and associated cancer mortality, have widened across socioeconomic groups. A population-based cohort study in Canada showed that socioeconomic marginalisation is associated with an increased risk of death in patients with endometrial cancer.<sup>29</sup> Furthermore, socioeconomically-deprived females with endometrial cancer in North West England were considered more likely to develop fatal recurrence.<sup>30</sup> Differences in endometrial cancer survival according to socioeconomic deprivation have also been reported among patients with Stage I endometrial cancer in Germany.<sup>27</sup>

In addition to socioeconomic disparities, educational disparities play a role. Seidelin et al.<sup>31</sup> examined the association between level of education and survival in patients with endometrial cancer in Denmark, and stated that unexplained increased risk for death, after adjustment for prognostic factors, warrants increased attention for patients with limited education in all age groups throughout treatment and rehabilitation. Ray-Coquard emphasised that: “Healthcare disparities in patients with endometrial cancer are not simply due to race; it is a question of education, knowledge, and whether the patient understands the physician’s treatment and management recommendations.”

Ray-Coquard speculated that populations with limited education may not understand how their disease might progress, or the benefits of participating in a clinical trial, such as receiving new treatments compared with standard of care, and regular medical check-ups. This lack of knowledge may lead to anxiety in these patients about clinical trial participation. In this case, reticence to take part in clinical research is directly correlated with knowledge and education, rather than race or socioeconomic status. This issue can be addressed by educating healthcare professionals and patients about the benefits of taking part in a clinical trial, thus enabling informed decision-making. Educational initiatives could be based around known barriers to participation in clinical trials, including distrust of the medical profession; concerns about the consequences of trial participation; issues of privacy, confidentiality, or the handling of personal information; concern about not receiving appropriate therapy; and anxiety about the possibility of detection of something new and unpleasant.<sup>32</sup>

Mirza highlighted other socioeconomic issues that are important in gynaecological cancers, using vaccination for preventing cervical cancer as an example. The human papilloma virus vaccine for cervical cancer is registered in Eastern Europe, and is recommended for all young females; however, governments and local councils do not have the funds to provide vaccination for this population. Only those better-off families who can afford vaccination are able to secure it for their children, thus creating a clear socioeconomic inequity. Furthermore, Eastern European countries like Poland are not

poor enough to receive support for vaccination programmes from funding sources such as the Gavi fund (Geneva, Switzerland), which provides financial support to African and Latin American countries. Mirza described a ‘limbo’ in these Eastern European countries, in which the governments approve and recommend certain treatments, but cannot afford to supply the treatments to all those eligible: “The governments, the local councils, and most patients cannot pay for these treatments. Only the rich can afford them.”

## THE IMPORTANCE OF COMORBIDITY AND LIFESTYLE IN ENDOMETRIAL CANCER

According to Ray-Coquard, comorbidities, particularly diabetes, hypertension, and obesity,<sup>2,3,33-37</sup> are important factors that impact the incidence and outcomes of endometrial cancer. Unlike information on race, data on comorbidities are collected in clinical studies throughout Europe, hence the association between comorbidity and outcome in endometrial cancer can be evaluated. Ray-Coquard suggested that there is a strong correlation between comorbidity, race, and socioeconomic status.

The disparity in outcomes, including overall survival, in patients with endometrial cancer cannot be fully explained by socioeconomic status in Europe, because the treatment offered is the same for all patients with this cancer. Ray-Coquard described lifestyle as a crucial factor that increases the risk of endometrial cancer development and progression.<sup>38</sup> This is particularly relevant in populations with low socioeconomic status, which tend to include a greater proportion of individuals who smoke,<sup>39</sup> and/or have higher risk of diabetes,<sup>40</sup> hypertension,<sup>41</sup> and obesity.<sup>40</sup> Ray-Coquard suggested: “Lifestyle has a greater impact on overall survival than appropriate cancer care.”

Mirza outlined that patients with endometrial cancer and comorbidities such as diabetes and obesity may not be able to tolerate cancer treatments as well as patients who do not have these comorbidities. Therefore, lifestyle, including the quality and amount of food consumed, and level of activity, is an important

target to improve patient outcomes; however, “it is not that easy for patients to change their eating and exercise habits.”

## ACCESS TO ENDOMETRIAL CANCER TREATMENT

Mirza and Ray-Coquard pointed out that disparities in access to treatment in Europe differ from those in the USA. In the USA, only those individuals with healthcare insurance can access treatment, thus creating inequity based on socioeconomic status, which is also linked to race. By contrast, in Europe, healthcare is usually completely covered by the individual country’s national healthcare system; therefore, all patients are offered the same treatment, irrespective of race and socioeconomic status. With this equal access healthcare system, patients would only be excluded from treatment because of comorbidities or tolerability issues, rather than because they cannot afford it.

Ray-Coquard introduced the concept of territorial disparity in healthcare, in which the numbers of physicians, nurses, and other healthcare professionals do not completely cover the healthcare needs in all areas of a country, leading to disparities in the quality of healthcare between different areas (e.g., city versus rural). This disparity is likely to become increasingly significant in the context of the global shortage of physicians.<sup>42-44</sup> Indeed, Ray-Coquard indicated that territorial disparity may surpass socioeconomic disparity in terms of impact and importance. In line with this, Mirza described a clear difference in the quality of treatment that can be offered to patients from central Greenland compared with patients in the Danish capital, Copenhagen. Mirza clarified that this difference is not a socioeconomic disparity but more to do with territorial disparity, with patients from remote areas having fewer healthcare professionals and treatment options available to them than those living in a city. Ray-Coquard considered this inequity to be a key area of healthcare research that deserves attention.

## DISPARITIES IN ADHERENCE TO ENDOMETRIAL CANCER TREATMENT GUIDELINES

Adherence to National Comprehensive Cancer Network (NCCN) treatment guidelines is the standard of care for various cancers, and has been reported to be associated with survival benefits.<sup>45</sup> Racial-ethnic and neighbourhood socioeconomic disparities in adherence to NCCN treatment guidelines for endometrial cancer have been reported in studies conducted in the USA.<sup>45,46</sup> However, Mirza and Ray-Coquard underscored that in Europe, standard of care treatment and adherence to guidelines should not differ based on sociodemographics, and that all individuals should have access to cancer treatments, regardless of racial-ethnic or socioeconomic background.

Mirza and Ray-Coquard acknowledged that there are numerous studies in the literature highlighting treatment disparities in patients with endometrial cancer, particularly for Black versus White populations in the USA. For example, Barrington et al.<sup>47</sup> observed differences in chemotherapy refusal by race; however, treatment refusal accounted for only a small fraction of the total racial disparity in endometrial cancer survival. Other treatment disparities that have been reported include Black females with low-risk endometrial cancer were less likely to undergo hysterectomy than White females in a recent study by Taylor et al.,<sup>48</sup> and there were racial-ethnic disparities in endometrial cancer-related hysterectomy surgical outcomes in research by Felix et al.<sup>49</sup> In addition, in a Canadian study, social marginalisation was associated with decreased likelihood of having primary hysterectomy following cancer diagnosis, or having delayed surgery, among patients with endometrial cancer.<sup>50</sup>

Other studies conducted in the USA that have provided information on treatment disparities in patients with endometrial cancer are as follows. Differences in, or omission of, adjuvant treatment have been proposed to be major contributors to the disparity in survival between Black and White patients with high-grade endometrial cancer.<sup>51</sup> Furthermore, various non-cancer factors have been suggested to affect the delivery of adjuvant radiotherapy to older females with early-stage endometrial cancer in real-world oncology



practice, including geographical region, race, residing in rural areas or neighbourhoods with high poverty, and frailty.<sup>52</sup> In addition, females who undergo lymph node assessment, who receive care from gynaecological oncologists rather than non-gynaecological oncologists, or who are treated in larger academic hospitals, are more likely to undergo adjuvant radiotherapy.<sup>52</sup> There are also sociodemographic disparities in the receipt of fertility-sparing treatment and assisted reproductive technology among patients with a history of cervical, endometrial, or ovarian cancer.<sup>53</sup> Furthermore, NCCN recommends genetic evaluation of females with endometrial cancer in certain circumstances; however, Black patients with this disease have been reported to be less likely to receive genetic counselling compared with patients of other races.<sup>54</sup>

Ray-Coquard highlighted that the patient's personal circumstances and professional activity can be key factors leading to non-adherence to treatment guidelines in Europe. For example, Ray-Coquard has observed discrepancies between the treatment schedules recommended in the guidelines and the treatment received in reality by farmers in France. These farmers do not have much financial or practical support, and there is often no one else to take on the work in their absence. Therefore, taking time off work for regular chemotherapy or immunotherapy is not always feasible, particularly if there are issues on the farm and no one else is available to solve them. This problem impacts conformity to guidelines and creates treatment disparity, not because of race or ethnicity, but due to lack of practical support, financial pressures, and the socioeconomic priorities of the patient.

## ADDRESSING DISPARITIES IN PATIENTS WITH ENDOMETRIAL CANCER

The experts remarked that various ideas have been proposed by authors in the USA to address disparities in endometrial cancer according to race, including community-based partnerships with a focus on policy interventions,<sup>55</sup> community engagement and race-conscious approaches,<sup>56</sup> efforts to include Black females and other populations that are under-represented in endometrial cancer molecular profiling studies<sup>57</sup> and Phase I clinical trials,<sup>58</sup>

further research into biomarkers and drug targets focusing on different racial groups,<sup>59</sup> and multidisciplinary approaches.<sup>60</sup> In addition, Miller et al.<sup>61</sup> noted that although there are a growing number of tools that can assist patients, caregivers, and clinicians in navigating the various phases of cancer survivorship, further evidence-based strategies and equitable access to available resources are needed to mitigate disparities, and optimise care for individuals with a history of cancer.

Ray-Coquard proposed that education and prevention are vital strategies to reduce or resolve disparities in patients with, or at risk of, endometrial cancer in Europe, and to prevent or reduce the incidence of comorbidities. In the USA, patients with endometrial cancer from deprived or underrepresented populations may be willing to participate in clinical trials because that is the only way in which they can access treatment. In Europe, where access to treatment is usually more straightforward, educating patients with endometrial cancer about their disease and the benefits of clinical research is crucial to maximise the likelihood of them agreeing to participate in molecular profiling studies, or early stage clinical trials.

Mirza emphasised: "In Western Europe, the governments and society should be making maximum effort to promote healthy lifestyle, including healthy eating, and smoking cessation. Reducing the occurrence of obesity, diabetes, and cigarette smoking will create a much healthier society overall, which, in turn, may decrease the occurrence of endometrial cancer, and improve patient outcomes."

## FUTURE PROSPECTS AND CONCLUSIONS

Ray-Coquard concluded that comorbidity accounts for some of the disparity in outcomes for patients with endometrial cancer. Education about endometrial cancer, healthy lifestyle, and preventative strategies to decrease comorbidity rates will help reduce the disparity between Black and White patients, and between patients with low and high socioeconomic status.

Mirza commented that statistics from the USA show that Black females have a higher incidence

of high-risk endometrial cancer than White females, and that this has not been adequately researched. Further work is needed to improve treatment outcomes for Black females with low socioeconomic status. New treatment modalities, including immune checkpoint inhibitors and poly(ADP-ribose) polymerase inhibitors, are

improving outcomes for patients with aggressive tumour types, and may provide better results in Black females in socioeconomically deprived populations. However, the issue of treatment access in the USA needs to be addressed to ensure eligible patients can receive these potentially effective treatments.

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