

Mammographic screening: hero or villain

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INTRODUCTION

In narratives, both real and fictional, characters and concepts often tread the fine line between heroism and its antithesis. This is the case with Felonius Gru from *Despicable Me*, and similarly, this concept can be applied to primary breast cancer (BC) screening examination: mammography. Both occupy the space of the “anti-hero,” embodying characteristics that challenge the traditional notions of heroism.

The portrayal of Gru in *Despicable Me* is a classic example of an anti-hero. Initially, he is driven by ambitions, anti-social tendencies, and malevolence, plotting grand heists, such as stealing the moon¹. However, beneath this villainous exterior lies a character filled with insecurities stemming from a childhood marked by abandonment and a longing for maternal validation. As the narrative unfolds, Gru's trajectory, influenced by the love of his three adopted daughters, sways toward redemption². This complexity, oscillating between villainy and virtue, makes Gru an anti-hero par excellence. His journey exemplifies the transformative power of experiences and evolving beliefs³.

In medical science, mammographic screening enables the early detection of cancer, offering treatment that is generally more effective, potentially curative, less complex, and less costly⁴. Mammographic screening has proven efficacy in reducing mortality from BC⁵⁻⁷, diagnosing the disease at less advanced stages^{8,9}, reducing the need for mastectomies, requiring less frequent axillary dissections, and leading to more limited use of chemotherapy^{8,10,11} when compared to unscreened women.

However, it is also associated with undesirable effects, such as false-positive results, overdiagnosis¹², radiation-induced BC^{13,14}, and potential psychological distress^{15,16}. Due to these factors,

the role of population screening has been debated^{15,17}, leading to controversies regarding the age to begin and end screening and its frequency^{18,19}.

While discussing mammographic screening, it is important to understand that its central idea is the identification of subclinical lesions aimed at early disease detection, thereby increasing the chances of successful treatment and consequently reducing mortality. The effectiveness of BC screening, and that of other diseases, can diminish the moment treating a clinical disease makes no difference from treating a subclinical disease²⁰.

With the introduction of very effective adjuvant therapies for BC, there has been increasing speculation about the relative contribution of screening versus therapy to the observed reduction in BC mortality and whether the importance of early detection in reducing deaths due to BC will diminish as new therapies are introduced²¹. Nowadays, most national and international guidelines recommend annual or biennial mammographic screening between 40 and 74 years for average-risk populations and annual mammography or annual magnetic resonance imaging starting from a younger age for high-risk populations¹⁹.

Given the above, we bring a discussion on the role of mammographic screening in the female population and its position as either a hero or a villain in medical science.

MAMMOGRAPHIC SCREENING AS A HERO

The mammographic screening has been extensively tested in numerous clinical trials²² and has also been evaluated in a recent meta-analysis using artificial intelligence²³. The practice of using mammograms to detect BC early has several key benefits:

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Mortality reduction

Early detection through mammography can improve survival rates because cancers can be found when they are smaller and are more treatable, and this has been consistently shown in several different studies^{21,24-28}.

Early diagnosis with the identification of early-stage tumors: Mammograms can identify BC before symptoms appear, leading to the detection of smaller tumors¹². This early detection in turn can lead to earlier treatment, which is often less aggressive and more likely to be successful⁵.

Decreased likelihood of needing radical surgery

When BC is caught early, there is a higher chance that a woman might undergo breast-conserving surgery (like lumpectomy) rather than more drastic measures, such as mastectomy⁵. Screening mammography has doubled the number of cases of early-stage BC that are detected each year in the United States²⁹.

Decrease of adjuvant treatment

Detecting cancer early can decrease the need for adjuvant treatment, including less invasive surgeries and the potential for avoiding chemotherapy³⁰. Genomic testing, especially in early BC, helps in avoiding overtreatment and focusing on treatments that provide the actual benefit³¹.

Cost-effectiveness

From a health economics perspective, screening can be cost-effective in terms of medical costs saved by early cancer detection and treatment, potentially leading to reduced healthcare spending on advanced cancer treatments^{32,33}.

MAMMOGRAPHIC SCREENING AS A VILLAIN

On the other hand, we have some points that can be considered problematic and can eventually disrupt patients' lives during screening:

Overdiagnosis

Overdiagnosis is defined as BC detected through screening that would not have become clinically apparent during a woman's lifetime with usual care. The main harm of overdiagnosis is related to the associated treatment^{16,34}.

The magnitude of overdiagnosis is controversial¹⁶. There is an extremely wide range (0-54%) of overdiagnosis estimates related to screening^{5,6,16,22}.

The rates of overdiagnosis in randomized trials were 11-22%¹⁶. It is projected that among women aged 50-74 years who are

screened biennially, about one in every seven cases of cancer detected through screening is overdiagnosed³⁵. For every BC death prevented, approximately five overdiagnosed cases will be managed⁵.

Ductal carcinomas in situ are the most common cause of overdiagnosis and should not be overtreated. Overdiagnosis is a much bigger problem in older women than in younger women, due to more competing causes of death at older ages¹¹.

Despite extensive research, the measurements used to estimate overdiagnosis have some limitations, and the prospective prediction of an overdiagnosed cancer at an individual level is not possible³⁶. It is impossible to know whether a specific lesion will progress and what its effect on a woman's health will be. Studies are highly heterogeneous, and estimates vary depending on the analytical approach. Until methodological standards for estimating overdiagnosis are more clearly defined, the correct estimate remains uncertain¹⁶.

Women who are overdiagnosed may be harmed by unnecessary procedures and treatments and by the burden of receiving a cancer diagnosis¹⁶. However, limiting diagnosis to symptomatic diseases is contrary to many aspects of contemporary medicine, which seeks to prevent symptomatic diseases through the successful diagnosis and treatment of pre-symptomatic conditions, even if this increases the incidence³⁴. Furthermore, ongoing advances in the personalized treatment of recently diagnosed cancer cases will decrease the significance of overdiagnosis by reducing treatment morbidity³⁴.

False-positive biopsy results

The cumulative risk of undergoing fine-needle aspiration cytology, core-needle biopsy, and surgical intervention with benign results due to screening is 3.9%, 1.5%, and 0.9%, respectively³⁷.

False-positive biopsy results occur when the decision to recommend a biopsy leads to a benign pathological outcome. The frequency of false-positive biopsy recommendations is 7.0-9.4% per decade of annual screening, depending on the age at the start. A woman screened annually would expect to receive a false-positive biopsy recommendation approximately once every 106-143 years of annual screening³⁴.

A systematic review observed that the 10-year cumulative rates of false-positive biopsy results were higher with annual screening compared to biennial (7 vs. 5%, respectively) for women aged 40-49 years, those with dense breasts, and those using combined hormone therapy¹⁶.

Radiation-induced breast cancer

Radiation-induced BC from mammographic screening and its incidence and mortality are influenced by the variability of the

screening dose, subsequent diagnostic investigation, age at the start, and frequency of screening. Women with large breasts may have a higher risk of radiation-induced BC¹⁴.

The number of lifetime cases of radiation-induced BC and the consequent deaths reflect differences in the doses used according to the type of technology³⁸. The radiation dose used depends on age, breast density, and breast thickness¹³.

For a dose of 2.5 mGy, the total lifetime risk of radiation-induced BC is 10 cases per 100,000 women if they were followed up from 50 to 85 years of age. The number of radiation-induced BC deaths is 1, and the assumed number of lives saved is approximately 350³⁹.

Therefore, it can be concluded that the risk of radiation-induced BC and related mortality from mammographic screening is minimal in comparison to the number of BC deaths it prevents^{13,39}.

CONCLUSION

The ability of mammography to detect potential threats early, combined with technological advancements that refine its

accuracy, underscores its irreplaceable role in modern medical science. A comprehensive understanding of mammography, including its negative and positive aspects, is essential. Recognizing its possible drawbacks while simultaneously capitalizing on its life-saving capabilities ensures the best outcomes for patients. Bringing together these narratives, the character of Gru and mammography, each in their unique way, challenge our traditional perceptions. Gru's evolution from a villain driven by egoistic ambitions to a loving father mirrors the nuanced understanding required for mammography. Both, while offering immense value, bring their inherent challenges, capturing the essence of the anti-hero.

AUTHORS' CONTRIBUTIONS

RFJ: Conceptualization, Data curation, Formal Analysis, Writing – original draft. **AFBMR:** Data curation, Formal Analysis, Writing – original draft. **LFC:** Data curation, Formal Analysis, Writing – original draft. **RBJ:** Data curation, Formal Analysis, Writing – original draft. **AM:** Data curation, Formal Analysis, Writing – original draft.

REFERENCES

- Adrianus C. Gru's character development in Despicable Me 1 Movie. 2015. Available from: <https://text-id.123dok.com/document/7d767jy-gru-s-character-development-in-despicable-me-1-movie.html>
- Tabentane R, Suprajitno S. Converted villain: a study on Gru's changing character traits in despicable me. 2015. Available from: <http://www.cbc.ca/news/arts/j-k-rowling-to-pen-harry-potter-spinoff-film-series-1.1701754>
- Dweck CS. Can personality be changed? The role of beliefs in personality and change. *Curr Direct Psychol Sci*. 2008;17(6):391-4. <https://doi.org/10.1111/j.1467-8721.2008.00612.x>
- World Health Organization. Guide to cancer early diagnosis. 2017. p. 1-48. Available from: <http://apps.who.int/bookorders>
- Canelo-Aybar C, Ferreira DS, Ballesteros M, Posso M, Montero N, Solà I, et al. Benefits and harms of breast cancer mammography screening for women at average risk of breast cancer: a systematic review for the European Commission Initiative on Breast Cancer. *J Med Screen*. 2021;28(4):389-404. <https://doi.org/10.1177/0969141321993866>
- Marmot MG, Altman DG, Cameron DA, Dewar JA, Thompson SG, Wilcox M. The benefits and harms of breast cancer screening: an independent review. *Br J Cancer*. 2013;108(11):2205-40. <https://doi.org/10.1038/bjc.2013.177>
- World Health Organization. Cancer. 2022. Available from: <https://www.who.int/news-room/fact-sheets/detail/cancer>
- Ahn S, Wooster M, Valente C, Moshier E, Meng R, Pisapati K, et al. Impact of screening mammography on treatment in women diagnosed with breast cancer. *Ann Surg Oncol*. 2018;25(10):2979-86. <https://doi.org/10.1245/s10434-018-6646-8>
- Puliti D, Bucci L, Mancini S, Paci E, Baracco S, Campari C, et al. Advanced breast cancer rates in the epoch of service screening: the 400,000 women cohort study from Italy. *Eur J Cancer*. 2017;75:109-16. <https://doi.org/10.1016/j.ejca.2016.12.030>
- Coldman AJ, Phillips N, Speers C. A retrospective study of the effect of participation in screening mammography on the use of chemotherapy and breast conserving surgery. *Int J Cancer*. 2007;120(10):2185-90. <https://doi.org/10.1002/ijc.22545>
- Yaffe MJ, Jong RA, Pritchard KI. Breast cancer screening: beyond mortality. *J Breast Imaging*. 2019;1(3):161-5. <https://doi.org/10.1093/jbi/wbz038>
- Welch HG, Prorok PC, O'Malley AJ, Kramer BS. Breast-cancer tumor size, overdiagnosis, and mammography screening effectiveness. *N Engl J Med*. 2016;375(15):1438-47. <https://doi.org/10.1056/NEJMoa1600249>
- Hooshmand S, Reed WM, Suleiman ME, Brennan PC. A review of screening mammography: the benefits and radiation risks put into perspective. *J Med Imaging Radiat Sci*. 2022;53(1):147-58. <https://doi.org/10.1016/j.jmir.2021.12.002>
- Miglioretti DL, Lange J, Broek JJ, Lee CI, Ravesteyn NT, Ritley D, et al. Radiation-induced breast cancer incidence and mortality from digital mammography screening: a modeling study. *Ann Intern Med*. 2016;164(4):205-14. <https://doi.org/10.7326/M15-1241>
- Gøtzsche PC, Jørgensen KJ. Screening for breast cancer with mammography. *Cochrane Database Syst Rev*. 2013;2013(6):CD001877. <https://doi.org/10.1002/14651858.CD001877.pub5>
- Nelson HD, Pappas M, Cantor A, Griffin J, Daeges M, Humphrey L. Harms of breast cancer screening: systematic review to update the 2009 U.S. Preventive Services Task Force recommendation. *Ann Intern Med*. 2016;164(4):256-67. <https://doi.org/10.7326/M15-0970>

17. Broeders M, Moss S, Nyström L, Njor S, Jonsson H, Paap E, et al. The impact of mammographic screening on breast cancer mortality in Europe: a review of observational studies. *J Med Screen*. 2012;19(Suppl 1):14-25. <https://doi.org/10.1258/jms.2012.012078>
18. Woloshin S, Jørgensen KJ, Hwang S, Welch HG. The new USPSTF mammography recommendations - a dissenting view. *N Engl J Med*. 2023;389(12):1061-4. <https://doi.org/10.1056/NEJMp2307229>
19. Ren W, Chen M, Qiao Y, Zhao F. Global guidelines for breast cancer screening: a systematic review. *Breast*. 2022;64:85-99. <https://doi.org/10.1016/j.breast.2022.04.003>
20. Maxim LD, Niebo R, Utell MJ. Screening tests: a review with examples. *Inhal Toxicol*. 2014;26(13):811-28. <https://doi.org/10.3109/08958378.2014.955932>
21. Duffy SW, Tabár L, Yen AM, Dean PB, Smith RA, Jonsson H, et al. Mammography screening reduces rates of advanced and fatal breast cancers: results in 549,091 women. *Cancer*. 2020;126(13):2971-9. <https://doi.org/10.1002/cncr.32859>
22. Flemman AF. Overdiagnosis due to screening mammography for breast cancer among women aged 40 years and over: a systematic review and meta-analysis. *J Pers Med*. 2023;13(3):523. <https://doi.org/10.3390/jpm13030523>
23. Liu J, Lei J, Ou Y, Zhao Y, Tuo X, Zhang B, et al. Mammography diagnosis of breast cancer screening through machine learning: a systematic review and meta-analysis. *Clin Exp Med*. 2023;23(6):2341-56. <https://doi.org/10.1007/s10238-022-00895-0>
24. Caswell-Jin JL, Sun LP, Munoz D, Lu Y, Li Y, Huang H, et al. Analysis of breast cancer mortality in the US-1975 to 2019. *JAMA*. 2024;331(3):233-41. <https://doi.org/10.1001/jama.2023.25881>
25. Berry DA, Inoue L, Shen Y, Venier J, Cohen D, Bondy M, et al. Modeling the impact of treatment and screening on U.S. breast cancer mortality: a Bayesian approach. *J Natl Cancer Inst Monogr*. 2006;(36):30-6. <https://doi.org/10.1093/jncimonographs/lgi006>
26. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med*. 2005;353(17):1784-92. <https://doi.org/10.1056/NEJMoa050518>
27. Duffy SW, Tabár L, Yen AM, Dean PB, Smith RA, Jonsson H, et al. Beneficial effect of consecutive screening mammography examinations on mortality from breast cancer: a prospective study. *Radiology*. 2021;299(3):541-7. <https://doi.org/10.1148/radiol.2021203935>
28. Huang X, Li Y, Song J, Berry DA. A Bayesian simulation model for breast cancer screening, incidence, treatment, and mortality. *Med Decis Making*. 2018;38(1_Suppl):78S-88S. <https://doi.org/10.1177/0272989X17714473>
29. Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence. *N Engl J Med*. 2012;367(21):1998-2005. <https://doi.org/10.1056/NEJMoa1206809>
30. Kerr AJ, Dodwell D, McGale P, Holt F, Duane F, Mannu G, et al. Adjuvant and neoadjuvant breast cancer treatments: a systematic review of their effects on mortality. *Cancer Treat Rev*. 2022;105:102375. <https://doi.org/10.1016/j.ctrv.2022.102375>
31. Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. *N Engl J Med*. 2018;379(2):111-21. <https://doi.org/10.1056/NEJMoa1804710>
32. Shih YT, Sabik LM, Stout NK, Halpern MT, Lipscomb J, Ramsey S, et al. Health economics research in cancer screening: research opportunities, challenges, and future directions. *J Natl Cancer Inst Monogr*. 2022;2022(59):42-50. <https://doi.org/10.1093/jncimonographs/lgac008>
33. Ratushnyak S, Hoogendoorn M, Baal PHM. Cost-effectiveness of cancer screening: health and costs in life years gained. *Am J Prev Med*. 2019;57(6):792-9. <https://doi.org/10.1016/j.amepre.2019.07.027>
34. Helvie MA, Bevers TB. Screening mammography for average-risk women: the controversy and NCCN's position. *J Natl Compr Canc Netw*. 2018;16(11):1398-404. <https://doi.org/10.6004/jnccn.2018.7081>
35. Ryser MD, Lange J, Inoue LYT, O'Meara ES, Gard C, Miglioretti DL, et al. Estimation of breast cancer overdiagnosis in a U.S. breast screening cohort. *Ann Intern Med*. 2022;175(4):471-8. <https://doi.org/10.7326/M21-3577>
36. Paci E, EUROSCREEN Working Group. Summary of the evidence of breast cancer service screening outcomes in Europe and first estimate of the benefit and harm balance sheet. *J Med Screen*. 2012;19(Suppl 1):5-13. <https://doi.org/10.1258/jms.2012.012077>
37. Hofvind S, Thoresen S, Tretli S. The cumulative risk of a false-positive recall in the Norwegian Breast Cancer Screening Program. *Cancer*. 2004;101(7):1501-7. <https://doi.org/10.1002/cncr.20528>
38. Freitas-Junior R, Correa R, Peixoto J-E, Ferreira RS, Tanaka RMN, et al. Abstract P3-01-07: estimated risk of radiation-induced breast cancer from mammographic screening. *Cancer Res*. 2012;72(24_Supplement):P3-01-07. <https://doi.org/10.1158/0008-5472.SABCS12-P3-01-07>
39. Hauge IH, Pedersen K, Olerud HM, Hole EO, Hofvind S. The risk of radiation-induced breast cancers due to biennial mammographic screening in women aged 50-69 years is minimal. *Acta Radiol*. 2014;55(10):1174-9. <https://doi.org/10.1177/0284185113514051>

