

What about the guys? An assessment of gender differences in hereditary colorectal cancer testing

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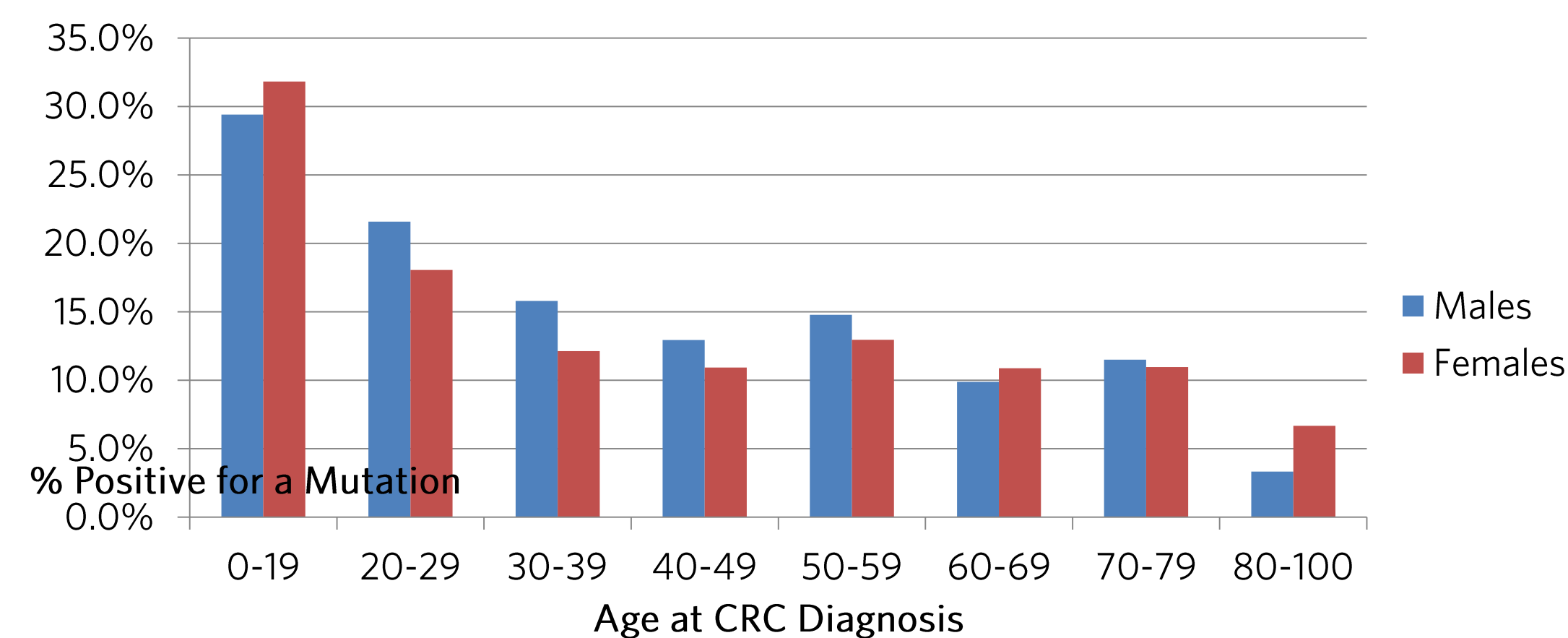
BACKGROUND

Approximately 5-10% of colorectal cancer (CRC) is due to hereditary causes. Identification of an inherited cause may impact surgical and treatment decisions for CRC patients and may identify increased risks for other cancers that warrant increased screening and/or risk reduction measures.^{1,2} Men have testing for hereditary breast and ovarian cancer less often than women,³ even though these genes may also cause increased risk for cancer in men and men are as likely as women to carry mutations in these genes and pass them onto their children. We aimed to explore whether similar gender differences exist related to testing for hereditary CRC.

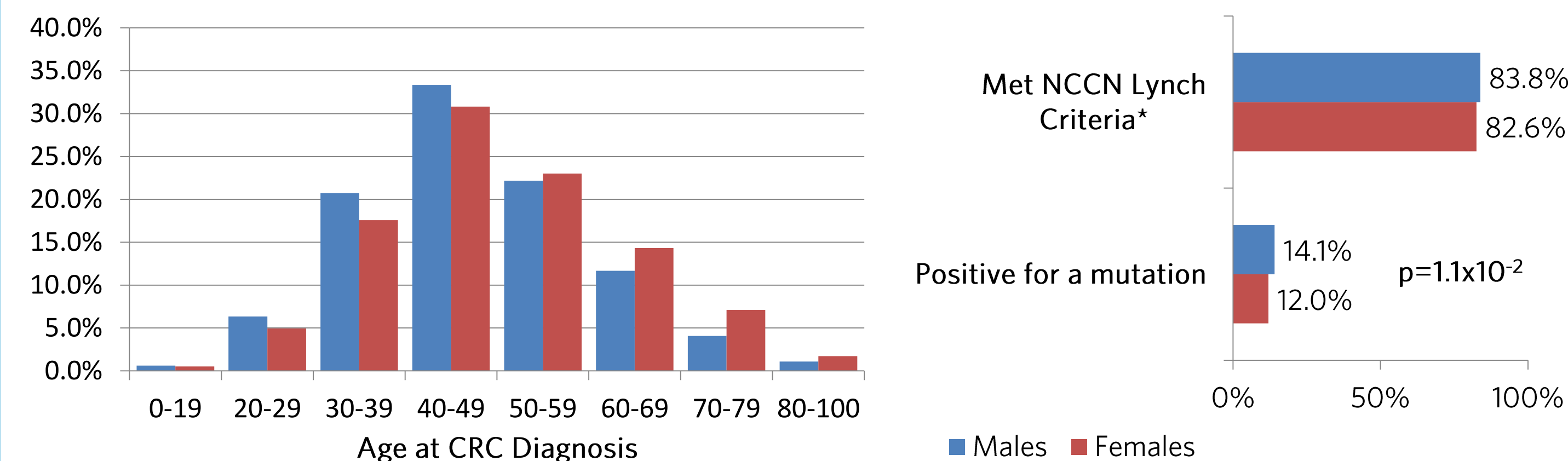
METHODS

- We retrospectively reviewed clinical data and test results from consecutive CRC cases, who had a multi-gene panel with 13-49 genes at our laboratory, between March 2012 and June 2016.
- Statistical comparisons between males and females were conducted using Fisher's exact test.

Positive Rates by Age at CRC Diagnosis



Cohort Characteristics, Males vs. Females



*NCCN criteria for Lynch syndrome genetic testing

RESULTS SUMMARY

- 7142 individuals with CRC had a multi-gene panel during the study period
 - 61.1% (n=4363) female, avg. age of diagnosis, 49.5 years
 - 38.9% (n=2279) male, avg. age of diagnosis, 47.2 years
 - 12.8% (n=914) positive for mutation or likely pathogenic variant
- Mutations in *CHEK2*, *MLH1*, and *MSH2* were most frequent in both men and women
- Women with CRC before age 20 had the highest mutation rate (31.8%), but men were more likely to test positive than women overall (14.1% vs 12.0%, $p=1.1 \times 10^{-2}$)
- Men and women were equally likely to meet NCCN guidelines for Lynch syndrome genetic testing ($p=1.6 \times 10^{-1}$)
- The only genes with significantly different mutation rates between men and women were *MLH1* (3.2% vs 1.5%, $p=2.0 \times 10^{-6}$) and *MSH6* (1.7% vs 0.8%, $p=3.0 \times 10^{-3}$)

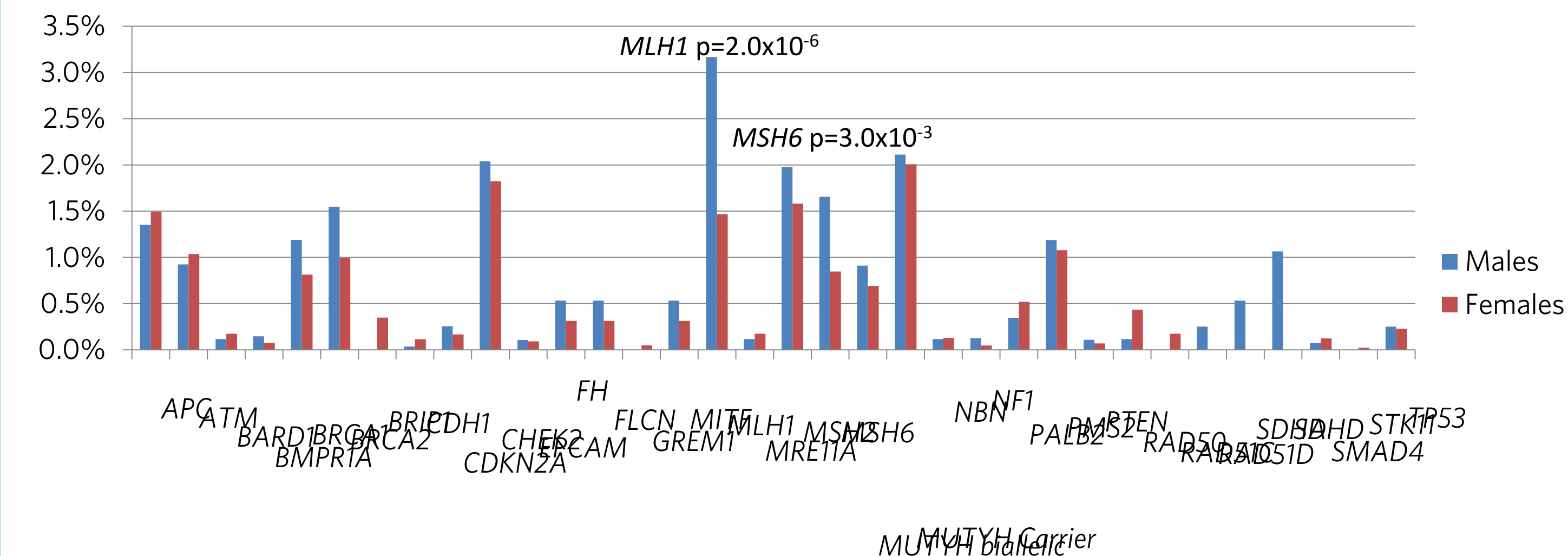
CONCLUSIONS

- While more women underwent genetic testing, men were more likely to test positive.
- Possible explanations include smaller sample size and earlier age of onset in men, perceptions of referring clinicians, and different levels of interest in genetic counseling and testing between male and female patients.
- These data highlight an important opportunity for education and identifying more men with hereditary CRC who may benefit from genetic information.
- Further studies are needed to confirm these results and explore reasons for the gender differences.

REFERENCES

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3. Bowling L, Reineke P, McFarland RE, et al: Gender bias: Underdiagnosing hereditary cancer in men with prostate cancer. J Clin Oncol 34, 2016 (suppl; abstr 1545)
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Gene-Specific Mutation Rates



There were no significant differences in positive rates between men and women for genes other than *MLH1* and *MSH6*.