



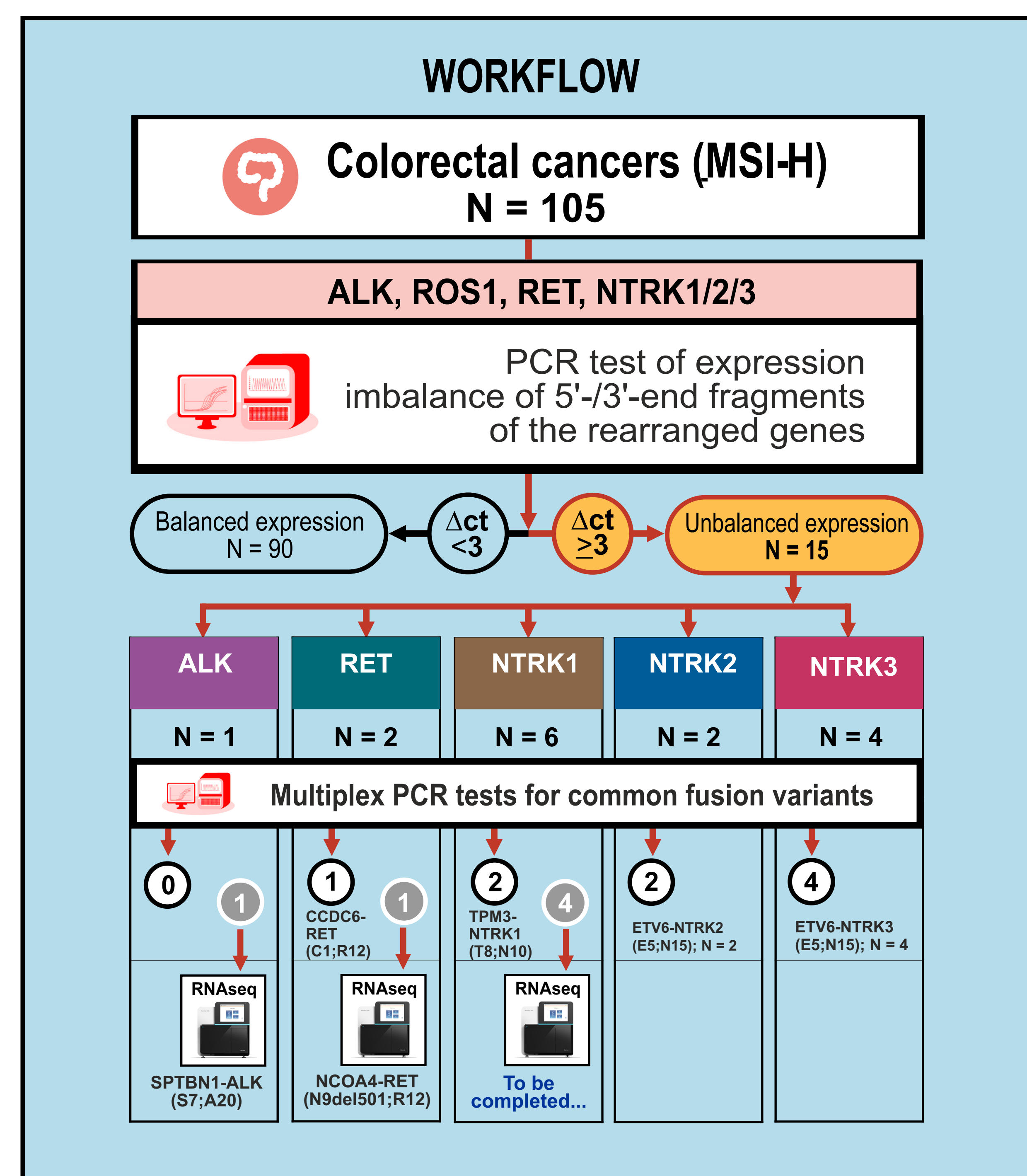
# 121P - Spectrum of druggable gene fusions in microsatellite-unstable colorectal tumors

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## Background & Purpose

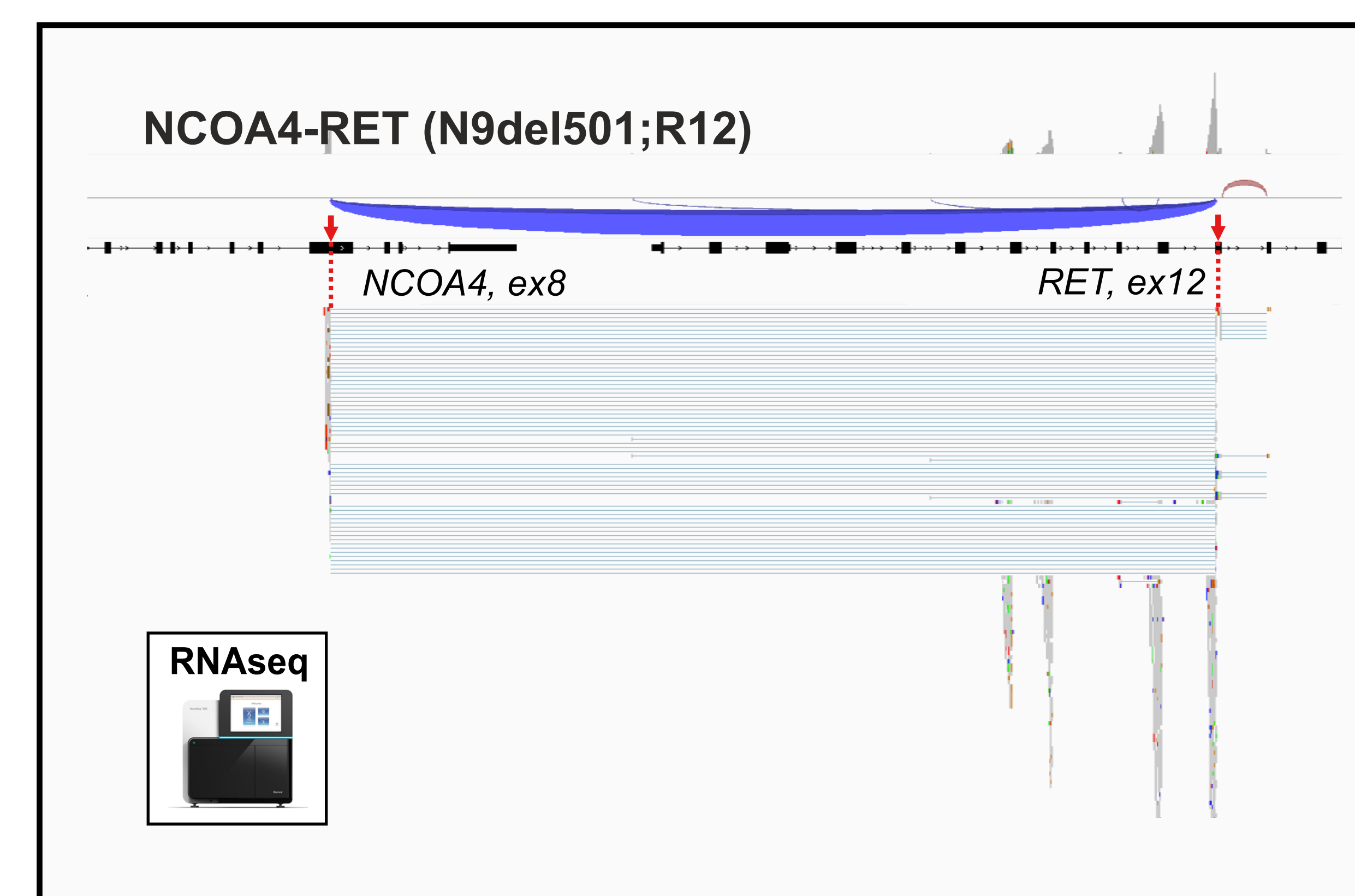
Colorectal carcinomas (CRCs) with high-level microsatellite instability (MSI-H) often contain gene fusions, which involve receptor tyrosine kinases. We aimed to determine the frequency of NTRK and other types of clinically relevant gene fusions in MSI+ CRC.



## Patients & Methods

The study included 105 MSI-H CRCs. NTRK1/2/3, ALK, ROS1 and RET gene fusions were analyzed by PCR test for 5'/3'-end unbalanced expression, which is capable of detecting all translocation variants.

The type of rearrangements was subsequently determined by variant-specific PCR for common fusions, and, whenever necessary, by targeted RNA next-generation sequencing (NGS).



## Results

NTRK1/2/3 translocations were the most common, being detected in 8/105 (8%) CRCs (TPM3-NTRK1 (T8;N10): n = 2; ETV6-NTRK2 (E5;N15): n = 2; ETV6-NTRK3 (E5;N15): n = 4).

There were 2 tumors with RET rearrangements (CCDC6-RET (C1;R12) and NCOA4-RET (N8del501;R12), respectively) and 1 instance of SPTBN1-ALK (S7;A20) chimera.

76/105 (72%) CRCs were negative for KRAS, NRAS or BRAF mutations.

Gene rearrangements were detected in 10 (13%) of these tumors. 29/105 (28%) carcinomas carried activating lesions in RAS/RAF oncogenes; one of these CRCs had both ETV6-NTRK3 (E5;N15) translocation and BRAF V600E substitution.

## Conclusions

**Microsatellite-unstable CRCs have high frequency of druggable gene rearrangements, with NTRK1/2/3 deserving particular attention.**

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**Conflict-of-interest statement:**  
**All authors have nothing to disclose**