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Increased testing for *Neisseria gonorrhoeae* with duplex nucleic acid amplification tests in Australia: implications for surveillance

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Abstract. ***Background*:** Gonorrhoea notifications have been increasing in Australia's cities, in both men and women. We investigated if this could be, at least in part, a result of a testing artefact. ***Methods*:** We surveyed 28 laboratories that were known to test for both *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) to determine their testing and reporting practices, and when these practices were instituted. ***Results*:** By 2012, 23 (82%) of the laboratories were routinely performing duplex nucleic acid amplification tests for both CT and NG even if a test for only one organism was requested, up from 9 (32%) laboratories before 2007. Although written reports of negative NG tests were not provided if the test was not requested, positive NG tests were always communicated to the attending clinician. ***Conclusions*:** The move towards routine duplex testing for CT and NG has probably resulted in more Australians being tested for NG than ever before. While this change has advantages for case-finding and improved public health outcomes, it also brings an increasing potential for false-positive NG tests. Recent trends in NG notifications should be interpreted with caution.

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Introduction

Australian gonorrhoea annual notifications have been rising substantially among men (from 5041 in 2007 to 9526 in 2012) and women (from 2594 in 2007 to 4116 in 2012), mainly in non-Indigenous people.[1] Much of the increase in diagnoses in men can be attributed to same-sex transmission,[1] but no explanation has been provided for the increase in women that has been focussed in urban areas.[2] Since the mid-2000s duplex nucleic acid amplification tests (NAAT) for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) have become available such that both organisms can be tested for on the same specimen at the same time. Under clinical guidelines[3] and from a low base,[4] testing for CT has risen sharply over recent years.[5] We had received anecdotal reports that some laboratories were routinely performing the duplex CT/NG NAAT tests even when a test for CT alone was requested. As most, but not all, of the increase in CT notifications can be explained by increased testing,[5] we investigated if the same could be happening for NG.

Methods

We surveyed by email the managers or delegates of the laboratories who participated in an Australian Society for Microbiology Special Interest Group, and those participating in the Australian Collaboration for Coordinated Enhance Sentinel Surveillance for Sexually Transmissible Infections and Blood Borne Viruses (ACCESS) project.[6,7] We asked each laboratory if they routinely performed a duplex CT/NG test if only a CT test was requested. If so, we asked them when they started routinely performing duplex tests, how they report the result, and who they informed if the NG test was positive.

Results

Of an estimated 35–40 laboratories likely to be testing for NG or CT in Australia, 28 of the larger laboratories responded. These laboratories, 10 private and 18 public, were based in every state and territory of mainland Australia. By the end of 2012, 23 (82%) of the 28 laboratories reported that they routinely used the duplex CT/NG NAAT test, up from 9 (32%) before 2007 (Fig. 1) even if a test for only one organism was requested. Eight different test platforms were reported, and two laboratories used in-house polymerase chain reaction tests. One laboratory only tested for NG by culture, which it only conducted on clinician request.

All of the 23 laboratories that performed routine duplex testing reported that they only provided a negative NG test

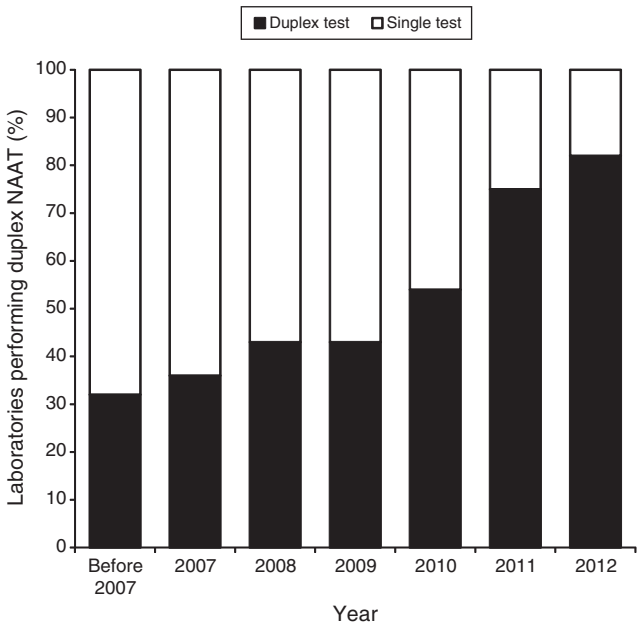

Fig. 1. Cumulative proportion of laboratories routinely performing a duplex nucleic acid amplification test (NAAT) for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* if only a test for *C. trachomatis* is requested, by year of commencement ($n = 28$).

result and billed Medicare for NG tests if NG testing was requested by the clinician. That said, all laboratories routinely performing duplex tests reported that they would contact the requesting clinician if the NG test was positive.

Discussion

Duplex testing for CT and NG has become routine in most Australian laboratories even if the clinician only requests a test for one organism. Duplex testing streamlines laboratory procedures, offsetting the slightly higher cost of the duplex test kits. However, routine duplex testing may have other implications.

First, the amount of NG testing of the Australian population must have increased several-fold in recent years, largely driven by the increase in requests for CT tests.[5] This increased testing would inevitably result in more diagnoses and an increase in NG notifications even if there was no change in the incidence or prevalence of NG. However, as these laboratories are not billing these NG tests through Medicare, an enhanced surveillance system would be required to determine trends in the testing denominator to enable interpretation of notification trends.

Second, some of these positive NG tests could be false-positive results, resulting in psychosexual and relationship harms,[8] although those harms are likely to be less severe for a readily curable infection than for a chronic infection. A limitation of this study was that we did not survey what confirmatory testing was performed in the event of a positive NG result, although confirmatory testing of positive NAAT tests for NG is recommended,[9] so we assume this was done routinely. Reference laboratories participating in the National Neisseria Network achieved an impressive specificity of 99.96% for molecular testing for NG using in-house confirmatory PCR tests.[10]

CT is much more common than NG in Australia's population centres,[1] with CT testing guidelines being predominantly age-based (16–29 years).[3] Testing for NG should be risk-based; however, routine duplex CT/NG testing results in large numbers of people at very low risk of NG being tested for NG. The prevalence of NG in women attending an inner city sexual health centre was just 0.37%,[11] and NG is known to be concentrated in such public clinics,[12] so it would be reasonable to assume a much lower prevalence of NG in most general practices, say, 0.037%. A confirmed NG test specificity of 99.96% and a true prevalence of 0.037% would net a positive predictive value of only 72.5%. That is, one-quarter of these positive tests in women could be false-positive results. False-positive NG tests could also undermine public health surveillance.

Our findings raise some interesting ethical issues. One view is that all tests should be preceded by informed consent. However, it could be readily argued that the patient that is consenting to be tested for chlamydia is, in practice, consenting to being tested for any readily curable sexually transmissible infection on the same specimen. Many women are unaware that a Pap smear is de facto also a test for trichomoniasis and human papillomavirus infection – and they are not routinely consented for this. Of course, this argument does not extend to HIV testing, which has more long-range implications for the patient.

Some respondents reported spontaneously that their laboratories serviced populations at high risk for NG such as gay men and Indigenous populations, so they therefore felt some public health obligation to test for NG even if only a CT test was requested. Undoubtedly some individuals who would have otherwise gone undiagnosed benefited as a result. It was notable that the laboratories unanimously felt an ethical obligation to communicate positive NG results to the requesting clinicians.

This study has limitations; these 28 laboratories may not be representative of all clinical laboratories in Australia though they were dispersed across seven jurisdictions, comprised most of the largest microbiology laboratories in Australia, and were split between public and private laboratories. Moreover, these data report number of laboratories, not number or proportion of tests conducted nationally. There are no public records of the numbers of laboratories performing CT/NG testing in Australia or the total number of NG tests performed.

In summary, in light of the expanding NG testing denominator and the unknown extent of false-positive tests, trends in NG diagnoses in the general population should be interpreted with caution. An enhanced laboratory-based surveillance system should be set in place.

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Conflict of interest

None declared.

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