Hyperacusis (also described as decreased, reduced, or collapsed sound tolerance) is a symptom that is attracting an increasing amount of interest, both clinical and research. Rather than describing extraordinarily sensitive hearing, like Superman being able to hear a whisper 200 metres away, hyperacusis is the experience of the world of sound becoming overwhelmingly intense, such that sound of even moderate intensity is perceived as hyper-intense, and in some cases, painful. Sub-categories of hyperacusis have been proposed [1], wherein it may be characterised by pain, loudness or fear: like all such frameworks there are issues with this, as the categories are not mutually exclusive, but the idea that emotion, auditory perception, and physical discomfort can be interwoven is compelling.

Misophonia is a different experience, though time will tell if there are similarities in the neurobiology of misophonia and hyperacusis. A person with misophonia will exhibit marked aversion to certain sounds, and the characteristic experience is of distress and disgust at the sound of family members eating. This is more common in adolescents and young adults, and can lead to major family tensions, with anger and rage being typical emotional reaction from the patient.

The growth of research activity in the fields is illustrated by Figure 1, in which the numbers of papers published each year with hyperacusis and misophonia as a keyword is indicated. Whilst unanswered questions regarding each condition abound, the increase in published research is encouraging as clinicians and researchers start to engage these experiences with serious intent, taking steps towards understanding, and eventually, truly effective treatments.

In this section of the Research Report the research published in 2016 on hyperacusis, and on misophonia is reviewed. Regarding hyperacusis alone, as the following analysis would not be meaningful for misophonia given the small number of papers,
a thematic analysis was performed. PubMed searching identified 43 papers on hyperacusis, and of these 26 were deemed to have a sufficient focus on decreased sound tolerance to be reviewed here. Figure 2 shows the numbers by the themes of mechanisms, aetiology, epidemiology, impact, and treatment. An interesting, and somewhat unexpected finding was that research attempting to identify mechanisms of hyperacusis was the frontrunner, although understanding the pathophysiology of the condition is an essential prerequisite step to understanding the natural history, and then the design of clinically and cost-effective treatment and interventions. These themes will now be used as a framework within which to reflect upon research in 2016.

**Figure 1**
Number of articles published in PubMed with hyperacusis or misophonia in the title, abstract or as a major topic per year

**Figure 2**
Number of articles published in PubMed with hyperacusis as a major focus, by theme

**Mechanisms**

Hidden hearing loss is a term that refers to a recently identified situation which can follow noise exposure, and may also be an early indicator of age-related hearing loss. For many years it was considered that the inner ear structures most vulnerable to noise, and to ageing, were hair cells, but attention has now turned to the synapses (neural connections) between the hair cells instead. It has been proposed that if these degenerate with age, or are damaged by noise, then hearing thresholds would not change – but that the ability to discriminate sound in background noise, and to perceive and tolerate loudness would deteriorate, changes in thresholds then following over time and further damage/degeneration. This phenomenon has been studied in animals [2], using a drug (carboplatin) that affects these synapses and this is of interest as this drug is used in some cancer treatments in humans. In a study involving humans, Liberman et al compared two groups of college students [3]. Both groups had normal hearing on pure tone audiometry on the usual frequencies tested (250Hz-8kHz), but one group had been exposed to very little noise, whilst the other had considerable noise exposure, and hence was at higher risk of hidden hearing loss (synaptic dysfunction/damage). The high risk group had hearing loss on high frequency audiometric testing (10-16kHz), poorer performance on word recognition tests in noise or with degraded speech, and abnormal findings on a diagnostic test of cochlear function (electrocochleography).

The authors inferred that this test battery has potential value in the diagnosis of hidden hearing
loss, and that hidden hearing loss may explain why some people had difficulty hearing in noisy situations. Liberman and colleagues also suggested that this synaptic damage may be one of a number of physiological contributors to the onset of tinnitus and/or hyperacusis. Niwa and colleagues noted that similar physiological patterns to that seen in hidden hearing loss were observed after blast injuries in rats [4], and also wondered if this might contribute to hyperacusis and tinnitus.

An alternate, though not necessarily contradictory, view about people exposed to loud sound who retain normal audiograms but who struggle to discriminate sound in background noise was proposed by Eggermont [5]. His perspective was on changes in the central auditory system (e.g. brain structures and networks involved in hearing), describing alterations in central gain (the way that the brain boosts quiet sound) and the frequency maps for sound in the cortex, which is where sound is analysed and interpreted. Such changes have long been associated with hyperacusis and tinnitus, and this promises to be a fruitful area for further research.

Longer term effects of noise exposure were investigated by a number of researchers. Clarkson and colleagues [6] considered the effects on the auditory brain of conductive hearing loss in rats. Such losses are common in human children with otitis media with effusion (glue ear), and so this is a topic of some interest. Clarkson and colleagues indicated that there were substantial adverse changes, including some that might lead to decreased sound tolerance, although they did not research any eventual recovery or remediation of those effects. Turner and Larsen [7] explored changes in the auditory behaviour of rats 12 months after intense sound stimulation, considering both tinnitus and hyperacusis, though this work focused more heavily on tinnitus than decreased sound tolerance.

A number of other themes regarding the mechanisms of hyperacusis were explored in 2016. Researchers in Nottingham [8] and New York [9] investigated the effects of large doses of salicylate (aspirin) in animals, which has previously been reported to induce tinnitus and/or hyperacusis, but a research group in Cleveland [10] reported results demonstrating how difficult it is to disentangle any possible experimentally induced tinnitus in an animal from any hyperacusis. This challenge was also the topic of a study by Knudson and Melcher [11] whose results indicate that the auditory startle response (ASR) in humans may not correspond to self-reported sound tolerance challenges, and hence question whether ASR can be used as a marker for hyperacusis in animal models.

Encouragingly, a variety of different perspectives are starting to be explored. The association between autism and sound tolerance issues has long been noted, though little empirical evidence has been gathered, but physiological research is next to nonexistent. A group of Japanese researchers [12] has begun to research sound sensitivity in a rat model of autism: their initial work indicates a potential failure of inhibitory progressing within the auditory brain. Discussion about mechanisms of sound-induced pain arose in work by Manohar et al [13], again drawing parallels between brain changes after noise induced hearing loss, and chronic pain signals.

Aetiology
Aetiology is the cause or causes of a disease or condition. When it comes to hyperacusis, many and multiple aetiologies have been proposed, and researchers are vigilant in this area. Viziano et al [14] investigated decreased sound tolerance in patients with Multiple Chemical Sensitivity (MCS), which is a chronic condition resulting from low-level chemical exposure. Audiometric thresholds and a measure of cochlear function were normal in the 18 patients studied, but self-report measures of sound tolerance were indicative of hyperacusis, and the authors proposed that this may be a central phenomenon. Fioretti et al [15] published a case report of a patient in whom hyperacusis was associated with photophobia, and with skin hypersensitivity: treatment with sound therapy, cognitive behaviour therapy, and with an antidepressant led to improvements in mood, and in the ability to tolerate both sound and light. Another case study [16] proposed that certain genetic variations found in a young female patient with autism may have been associated with her sensory sensitivities: whilst of interest, this is an emergent field of research. Degeest et al [17] presented questionnaire data from a series of 81 patients with troublesome tinnitus, indicating that the presence and extent of hyperacusis contributed to the self-reported handicap in this series, which fits clinical observations. Whilst each of these different perspectives is of interest, research on the causes of hyperacusis did not make substantial progress in 2016.
**Epidemiology**

Research into the prevalence, incidence, characteristics and natural history of disorders of decreased sound tolerance is extremely important in building our understanding of these symptoms and formulating effective treatment interventions. Knowledge and data regarding the epidemiology of hyperacusis is sparse, and there has been some research activity in this area published in 2016.

In a large scale general population questionnaire study from Sweden, Paulin et al.[18] found that of 3374 adult individuals who responded to the study invitation, 313 self-reported as having hyperacusis (9.3%), and 66 (2.0%) had been diagnosed with hyperacusis by a physician. Factors associated with hyperacusis included higher age, female gender, and higher educational status, and other medical conditions co-incident with hyperacusis included tinnitus, post-traumatic stress, chronic fatigue, pain syndromes, and hearing loss. Whilst not breaking new ground, this work does substantiate and build upon previous studies.

A systematic review [19] of tinnitus and hyperacusis in children and adolescents concluded that the data available contained so many methodological challenges that little in the way of firm evidence could be gleaned. Variability of definitions, questions asked, and populations studied with regard to age and hearing status, rendered comparison across studies meaningless. Studies published subsequently on tinnitus [20] and hyperacusis [21] on a cohort of approximately 7000 11 year olds in the UK indicated that 3.5% of the cohort experienced tinnitus that was persistent and bothersome, and that 3.7% reported hyperacusis. The report of hyperacusis was associated with female gender, higher maternal educational level, and readmission to hospital in the first 4 weeks of life. It has previously been noted that far fewer children with tinnitus and hyperacusis are seen in clinical practice than are detected by population studies, and Rosing et al.[22] indicated that very few children with tinnitus and/or hyperacusis are seen in clinics in Denmark, and those that are referred are in general seen in clinics primarily treating adults.

**Impact**

Only one research paper published in 2016 considered the impact of hyperacusis, and that investigated the impact upon hearing abilities rather than the psychosocial domains. Vielsmeier et al.[23] researched speech comprehension difficulties in patients with tinnitus, and found that the presence of hyperacusis was associated with poorer test performance in noise, but not in quiet environments. The authors proposed that a deficit in inhibition in the central auditory system might underlie both decreased sound tolerance and poorer speech comprehension in noise.

**Treatment**

The effectiveness of treatments for tinnitus and hyperacusis in the UK NHS were assessed by Aazh and colleagues [24]. Talking therapies were rated most highly, and sound therapies relatively lowly. There are a number of learning points here: first, that the opinion of patients about their treatment is highly important. Second, that is a substantial challenge to disentangle the effects of tinnitus and hyperacusis in research studies. Finally, this corroborates the view that sound therapies for both hyperacusis and tinnitus remain underdeveloped and under-evaluated, and there are some major opportunities in this area.

Silverstein et al.[25] reported the results of a surgical procedure for severe intractable hyperacusis that had been unresponsive to other therapy. Both the round and oval window of the cochlea were reinforced with other membranes in six patients (nine ears), and modest improvements on loudness discomfort testing was reported, alongside some improvement on questionnaire data. This observational study, though prospective, does not carry the same weight as a randomised controlled trial. Additionally, if the view that decreased sound tolerance is associated by increased central auditory gain has validity, then the same concerns about a surgical procedure that reduces auditory input to the cochlea would apply as to the long term chronic use of hearing protection in hyperacusis.
Misophonia
Surprisingly, given the amount of discussion about misophonia amongst audiologists and patient groups, only one research paper was published. Bruxner et al [26] present a case report and a review, coming from the perspective that misophonia is an under recognised psychiatric symptom, and giving it the sobriquet “mastication rage”. The debate about whether misophonia is essentially an audiological or a psychological disorder, or both, has further ground to cover, as does the quest for effective clinical interventions.

Discussion
Whilst it is encouraging that the research literature regarding hyperacusis is growing, and emanating from a number of different disciplines, there are a number of concerns. In 2016 a number of themes were entirely lacking, for example measurement and questionnaires, and natural history. The literature that does exist is often very specific, and potentially more concerned with the interests and concerns of the researcher/clinician rather than the patient community. In this latter regard the excellent work of Hyperacusis Research (www.hyperacusisresearch.org) should bear fruit in bring patient concerns to the forefront of research, and in providing a framework wherein researcher and clinicians can work together in a co-ordinated and comprehensive body of research.

The views expressed in this publication are those of the author(s) and not necessarily those of the National Institutes of Health, the National Institute for Health Research, or the Department of Health.

Conflict of interest:
David Baguley was an author on four of the papers mentioned herein. He is an Editor with Prof Marc Fagelson of a forthcoming book on hyperacusis, published by Plural Publishers in Autumn 2017.