Management of Vulval Pain

2014 UK national guideline on the management of vulval conditions
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Gulshan Sethi⁴ and Deepa Grover⁵

Honorary Life Fellow

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Consultant in Sexual Health & Menopause Specialist,
Bristol & Weston

Vice President
Multidisciplinary Approach to Diagnosis

PRINCIPLES OF CARE:
 Appropriately trained clinician(s)
 Information & Support
 Adequate clinical facilities
 Medical Photography
 Research Collaboration

TEAM:
 Gynae / Derm / SH / Pathol
 and
 • Psychosexual therapy
 • Pain management
 • Clinical psychology
 • Specialist physiotherapy
 • Reconstructive surgery
 • Continence advisory service
 • Oral physicians
 • Colorectal surgeons
Categories of Vulval Pain

ACUTE
- Covert
- Overt

CHRONIC Vulvodynia
- Unprovoked
  - “Generalised Vulvodynia”
- Provoked
  - Localised
  - Vestibulodynia

Infectious Dermatological

GV

LPV
Consensus Definition of Vulval Pain

Vulvar pain - caused by a specific disorder:
- Infectious - recurrent candidiasis, herpes, *candida*
- Inflammatory - lichen sclerosus, lichen planus, immunobullous disorders
- Neoplastic - Paget disease, squamous cell carcinoma
- Neurologic - postherpetic neuralgia, nerve compression, nerve injury, neuroma
- Traumatic - obstetric, female genital mutilation, cosmetic labiaplasty, HSV labial fusion
- Iatrogenic - postoperative, chemotherapy, radiation
- Hormonal - hypoestrogenic vulvovaginal atrophy, lactational amenorrhea, *Depo MPA*

Vulvodynia - vulvar pain >3 months without a clear identifiable cause:
- Localized - vestibulodynia, clitorodynia or generalized or mixed
- Provoked - insertional, contact or spontaneous or mixed
- Onset - primary or secondary
- Temporal - intermittent, persistent, constant, immediate, delayed

*Additions in yellow*

Categories of Vulval Pain

ACUTE

Covert Overt

Infectious Dermatological

CHRONIC

Vulvodynia

Unprovoked

“Generalised Vulvodynia”

Provoked

Localised Vestibulodynia

GV

LPV
Acute, Covert Vulval Pain

23y, nulliparous  LSI 1 week ago

12h Severe vulval pain, no trauma
   “Like being kicked by a horse”
   Copious clear watery vaginal Dx

Externally NAD

Photo  ©2003 P Greenhouse FRCOG
Acute, Covert Vulval Pain

23y, nulliparous    LSI 1 week ago

12h Severe vulval pain, no trauma
“Like being kicked by a horse”

Copious clear watery vaginal Dx

Externally NAD
Also has tender inguinal LNs

Herpetic Necrotic Cervicicitis
Assoc. w. S2 parasthesiae
Acute Retention of Urine
Nerve Distribution?

CUTANEOUS INNERVATION OF PELVIC FLOOR

- Iliohypogastric L1
- Ilioinguinal L1, Genitofemoral L2
- Pudendal S2,3,4
- Perineal S1,2,3
  (Br. of Posterior femoral cutaneous)
- Coccygeal plexus S5,Co1
- Medial cluneal S1,2,3
- Inferior cluneal S1,2,3
- Superior cluneal L1, 2, 3

S3/4/5

Photo ©1965 CS Nicol FRCP
Herpes or ..........?

38y, P2+1  Perimenopausal PMS

c/o Recurrent painful genital ulceration

just before each period

Sometimes associated with oral apthous ulceration

Photo ©2008 P Greenhouse FRCOG
Herpes or Behçet’s?
Behçet’s Disease
Behçet’s Disease

Photos ©2007 P Greenhouse FRCOG
Approx 15 different dermatological conditions with clear pre-menstrual trigger

[Perimenstrual dermatoses: a comment fact of chronobiology]
Piard-Franchimont C, Fraiture AL, Delvoye P, Dehavay J, Deleixhe-Mauhin F, Van Cauwenberge JR, Piard GE.
Categories of Vulval Pain

ACUTE
- Covert
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  - "Generalised Vulvodynia"
- Provoked
  - Localised
  - Vestibulodynia

Herpes
Behcet’s
Lichen Sclerosus
Lichen Planus
Paget’s, Lipschutz
Orogenital Apthous
(Hypoestrogenism)

GV

LPV
Lichen Sclerosus
Male Genital Lichen Sclerosus

- “Unequivocally a disease of the uncircumcised”
- Dyspareunia is common
- Non-specific histology – similar to women
- 1-2% malignancy risk – similar to women
- Most cured by topical ultrapotent steroid (~60%)

“Urine contact is overwhelmingly implicated in the pathogenesis”

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Clinical parameters in male genital lichen sclerosus: a case series of 329 patients
Edmonds EV, Hunt S, Hawkins D, Dinneen M, Francis N, Bunker CB.
Vulval Lichen Sclerosus

• “No consensus on underlying pathogenesis”

• ?? Urinary spillage as for men
Lichen Sclerosus

22y

Photo ©2002 P Greenhouse FRCOG

63y

Photo ©2007 P Greenhouse FRCOG
Lichen Planus

Erosive Type – Aggressive Idiopathic

Ulceration & loss of tissue
Oral (70%) & Genital lesions
Wickham’s striae

Diagnose by biopsy
Rx Dermovate

3% Premalignant – Vulval clinic FU
Lichen Planus

Erosive Type – Aggressive Idiopathic Ulceration & loss of tissue
Oral (70%) & Genital lesions
Wickham's striae
Diagnose by biopsy
Rx Dermovate
3%

3% Premalignant – Vulval clinic FU

Lichen Planus

Photo ©2014 P Greenhouse FRCOG

Photo ©2018 Fiona Lewis FRCP
Dewhurst's Textbook of Obstetrics & Gynaecology
Lichen Simplex

Vulval Psoriasis

Photo ©2001 P Greenhouse FRCOG

Photo ©2004 P Greenhouse FRCOG
Categories of Vulval Pain

ACUTE
- Covert
- Overt
  - Herpes
  - Behcet’s
  - Lichen Sclerosis
  - Lichen Planus
  - Paget’s
  - (Hypoestrogenism)

CHRONIC
- Vulvodynia
  - Unprovoked
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GV
LPV
PGAD
Persistent Genital Arousal Disorder
Persistent Genital Arousal Disorder (PGAD)

CAUSE
Sensory neuropathy in Dorsal Clitoral Nerve

DON’T
- Give SSRIs - Anorgasmia
- Give Botox
- Refer to Psychiatrist
- Pelvic Floor Exercises

DO
- Supportive / Empathetic approach
- Consider Rx:
  - Clonazepam / Lorazepam
  - Gabapentine
  - T.E.N.S.

WEBSITE

A Comparison of Medical Comorbidities, Psychosocial, and Sexual Well-being in an Online Cross-Sectional Sample of Women Experiencing Persistent Genital Arousal Symptoms and a Control Group.
Jackowich RA, Poirier É, Pukall CF.
Categories of Vulval Pain

ACUTE
- Covert
- Overt
- Herpes
- Behcet’s
- Lichen Sclerosus
- Lichen Planus
- Paget’s (Hypoestrogenism)

CHRONIC
- Vulvodynia
- Unprovoked
  “Generalised Vulvodynia”
- Provoked
  Localised Vestibulodynia

Unprovoked
- “Generalised Vulvodynia”
  GV
- GD:LPV ~ 1:10

LPV
Vulvodynia Definition

Vulvar pain of at least 3 months’ duration without clear identifiable cause

Potential associated factors:
• unresolved local inflammation
• nociceptive neuroproliferation
• central neurological mechanisms
• specific gene polymorphisms
Multidisciplinary Approach to Vulvodynia Diagnosis

Focus on:
- Pain History
- Sexual History
- Psychosexual Evaluation

Inspection:
- Exclude STI / Microscopy
- Exclude Derm. LS / LP
- Exclude obstetric trauma
- Cotton swab testing
- Pelvic Floor assessment

“ALL NEGATIVE”
“LOOKS NORMAL”

[ :: no photographs!]
# Vulvodynia “Treatment”

| Commonly used oral medications for management of generalized vulvodynia |
|---|---|---|
| **Name** | **Dosing** | **Titration** |
| TCAs | 10–100 mg/d (average 50–75 mg/d) | Start at 10–25 mg and titrate up by 10–25 mg every 7 d to max dose |
| Amitriptyline | | |
| Nortriptyline | | |
| Desipramine | | |
| Duloxetine | 20–60 mg/d | Start at 20 mg and titrate up by 20 mg/d every 7 d to max dose |
| Gabapentin | 100–3600 mg/d in 3 divided doses | Start at 100 mg and titrate up by 100 mg/d every 5–7 d if well-tolerated |
| Pregabalin | 150–300 mg/d in 2–3 divided doses | Start at 150 mg and titrate up by to 300 mg after 1 wk if well-tolerated |

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**Category** | **Examples**
---|---
Infectious | Recurrent candidiasis, herpes simplex virus
Inflammatory | Lichen planus, lichen sclerosis
Neoplastic | Paget disease, squamous cell carcinoma
Neurologic | Nerve compression, neuroma, postherpetic neuralgia
Trauma | Obstetric injury, female genital cutting
Iatrogenic | Radiation, postoperative
Hormonal | Genitourinary syndrome of menopause, lactational amenorrhea

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**Vulvodynia: Diagnosis and Management.**
Stenson AL.
Vulvodynia - Other Options?

CBT

Effectiveness of Cognitive-Behavioral Therapy and Physical Therapy for Provoked Vestibulodynia: A Randomized Pilot Study.
Goldfinger C, Pukall CF, Thibault-Gagnon S, McLean L, Chamberlain S.

Pelvic Floor Physiotherapy

Prendergast SA.

Physiotherapy for pelvic pain and female sexual dysfunction: an untapped resource.
Berghmans B.
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**Vulvodynia**
- Herpes
- Behcet’s
- Lichen Sclerosus
- Lichen Planus
- Paget’s
  - (Hypoestrogenism)

**GV**

**LPV**
“And now we look for joys to come...”

Thomas Rowlandson 1756-1827
Premier English Cartoonist
Localised Provoked Vestibulodynia

“Focal Vulvitis”
Peckham BM Am J OG 1986

“Vulvar Vestibulitis”
Friedrich EG J Reprod Med 1987
Localised Provoked Vestibulodynia

“Focal Vulvitis”
Peckham BM Am J OG 1986

“Vulvar Vestibulitis”
Friedrich EG J Reprod Med 1987
Localised Provoked Vestibulodynia

Swab touch test

Touch above
Localised Provoked Vestibulodynia

Swab touch test
Localised Provoked Vestibulodynia

Swab touch test

Touch on – pain score ? /10
Detailed Observation needed...
Localised Provoked Vestibulodynia

Pill Evidence
Bouchard 2002 / Greenstein 2007

Hormone Evidence
LeClair 2011 / Eva 2003

Hormone Treatment Evidence
Bayliss & Goldstein 2013 / Greenhouse 2011

Genetic Evidence
Goldstein 2014

Initial Management Pathway?
Could COC Pill cause HARM?

<table>
<thead>
<tr>
<th>Type of oral contraceptive used</th>
<th>Cases (n = 137)</th>
<th>Controls (n = 302)</th>
<th>Relative risk†</th>
<th>95% confidence interval</th>
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</thead>
<tbody>
<tr>
<td>Never used</td>
<td>5</td>
<td>52</td>
<td>1.0</td>
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</tr>
<tr>
<td>Progestogenic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>60</td>
<td>130</td>
<td>4.7</td>
<td>2.0, 15.1</td>
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<tr>
<td>High</td>
<td>26</td>
<td>35</td>
<td>2.8</td>
<td>1.6, 3.7</td>
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<tr>
<td>Mixed</td>
<td>46</td>
<td>85</td>
<td>2.5</td>
<td>1.4, 3.7</td>
</tr>
<tr>
<td>Premenstrual</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>35</td>
<td>59</td>
<td>7.7</td>
<td>2.7, 21.9</td>
</tr>
<tr>
<td>High</td>
<td>92</td>
<td>129</td>
<td>1.7</td>
<td>1.6, 2.1</td>
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<tr>
<td>Mixed</td>
<td>99</td>
<td>199</td>
<td>2.9</td>
<td>1.8, 4.8</td>
</tr>
<tr>
<td>Estrogenic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low only</td>
<td>39</td>
<td>87</td>
<td>4.9</td>
<td>1.8, 13.6</td>
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<tr>
<td>High only</td>
<td>38</td>
<td>63</td>
<td>8.0</td>
<td>2.8, 22.5</td>
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<tr>
<td>Mixed</td>
<td>38</td>
<td>100</td>
<td>2.7</td>
<td>1.7, 21.1</td>
</tr>
<tr>
<td>Androgenic</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low only</td>
<td>59</td>
<td>126</td>
<td>6.5</td>
<td>2.4, 17.8</td>
</tr>
<tr>
<td>High only</td>
<td>39</td>
<td>88</td>
<td>1.8</td>
<td>1.6, 19.5</td>
</tr>
<tr>
<td>Mixed</td>
<td>10</td>
<td>38</td>
<td>5.3</td>
<td>2.3, 13.8</td>
</tr>
</tbody>
</table>


Use of oral contraceptive pills and vulvar vestibulitis: a case-control study.
Could Progestagen do HARM?

More common in women taking COC with most androgenic progesterones

<table>
<thead>
<tr>
<th>Never used OC Pill</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest Risk Pill</td>
<td>3 (1.0 - 9.3)</td>
</tr>
<tr>
<td>Highest Risk Pill</td>
<td>19 (3.0 - 120)</td>
</tr>
</tbody>
</table>

Eg Norgestimate – EE35 “Cilest®” etc

Eg Levonorgestrel – EE30 “Microgynon®” etc

Use of oral contraceptive pills and vulvar vestibulitis: a case-control study
Progestagen Androgenicity

Androgenicity Index of Progestagens
(after Cibula D. ESC Prague 2008)
Levonorgestrel Androgenicity

Closest-derived progestogen to testosterone

? Specific risk of dysphoria (~25-30%)

LNG-dysphorics have gene locus SNPs

LNG-dysphorics have fMRI alterations

Greater risk of perimenopausal PMDD

Greater risk of PND / Puerperal Psychosis

Adverse mood symptoms with oral contraceptives
Does less Estrogen do HARM?

- 51% of Israeli women use low dose ≤20μg COC
- 49% use higher-dose estrogen 30-35μg COC

N=132 women with Secondary LPV

86 (65%) using COC Pill

Low dose 68 (79%) \( p < 0.002 \) vs control
High dose 18 (21%) \( p < 0.002 \) vs control

More women with LPV use low-dose estrogen than those who use high-dose estrogen pills

Vulvar vestibulitis syndrome & estrogen dose of oral contraceptive pill
## Coding for Androgen Receptor on X chromosome

Contraceptive-induced provoked vestibulodynia (CIPV) on DRSP-EE

<table>
<thead>
<tr>
<th></th>
<th>CIPV  n= 30</th>
<th>Control  n=17</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAG Repeat sequences</td>
<td>22.05 +/- 2.98</td>
<td>20.61 +/- 2.19</td>
<td>0.025</td>
</tr>
<tr>
<td>Mean Free Testosterone</td>
<td>0.127 +/- 2.98</td>
<td>0.189 +/- 2.19</td>
<td>0.042</td>
</tr>
</tbody>
</table>

“CIPV may be due to: lowered free testosterone and an inefficient Androgen Receptor predisposing women to vestibular pain”

Goldstein AT et al *J Sex Med* 2014;11:2764-71

Polymorphisms of the androgen receptor gene & hormonal contraceptive-induced provoked vestibulodynia
Localised Provoked Vestibulodynia

Pill Evidence
Bouchard 2002 / Greenstein 2007

Hormone Evidence
LeClair 2011 / Eva 2003

Genetic Evidence
Goldstein 2014

Hormone Treatment Evidence
Burrows & Goldstein 2013 / Greenhouse 2011

Initial Management Pathway?
LPV: Definitions

- **Primary** - since first sex
- **Secondary** - previous pain-free sex
- **Post – Menopausal**
  - Estrogen responsive
  - Estrogen non-responsive
Hormone Receptor changes

Secondary: previous pain-free sex

- Reduced Estrogen receptor – alpha
- Reduced Progesterone receptors


Are 1° & 2° LPV different?

Primary > Secondary

- Increased neural hypertrophy & hyperplasia
  
  (P=0.02, OR 3.01 95%CI 1.2-7.6)

- Increased progesterone receptor nuclear immunostaining
  
  (P=0.004, OR 3.94 95%CI 1.6-9.9)

- Estrogen receptor α expression (<5 years)
  
  (P=0.004, OR 5.53 95%CI 1.71-17.91)

Differences in primary compared with secondary vestibulodynia by immunohistochemistry
Progesterone receptors

Differences in primary compared with secondary vestibulodynia by immunohistochemistry
Are hormones involved?

Appearance & histology similar to post-menopausal hypoestrogenic vulval atrophy?
Could hormones help?

Appearance & histology similar to post-menopausal hypoestrogenic vulval atrophy?

59y woman c/o dyspareunia after GP stopped HRT

Completely resolved after Rx Vaginal estrogen pessaries

Divide into
- Estrogen responsive
- Estrogen non-responsive

Histopathologic characteristics of menopausal vestibulodynia
Switching hormones HARMS?

41y p1+1
Prior pain-free intercourse 6 years

“Too old for the Pill”
Rx Depoprovera  2 years 4 months
LPV Dyspareunia  2 years

Pain Score  
17 → 2
Switching hormones HARMS?

25y p0+1

Prior pain-free intercourse 18 m.

Pain Score

18 ➔ 0

Migraine with aura  8 months ago
Switched from COC Pill to Desogestrel POP
LPV Dyspareunia  5 months
Localised Provoked Vestibulodynia

Pill Evidence
Bouchard 2002 / Greenstein 2007

Hormone Evidence
LeClair 2011 / Eva 2003

Genetic Evidence
Goldstein 2014

Hormone Treatment Evidence
Burrows & Goldstein 2013 / Greenhouse 2011

Initial Management Pathway?
“Logical” treatment of LPV?

Hypoestrogenism causes LPV in some W.

Reaction to androgenic contraception is genetically predetermined

- Change contraceptive hormones?
- Give local estrogen?
Rx: Estrogen & Testosterone

Introital Estradiol + Testosterone cream  n=50

Mixed COC Pills used:
- Drosperinone-EE20/30 (Yaz/Yazmin) =11
- Norethisterone-EE20/30 (LoEstrin) =6
- Other brands -EE20/30/35 =33

Highest Vestibular Pain Score (max 10)

Burrows LJ, Goldstein AT. Sex Med. 2013; 1: 30–33
The treatment of vestibulodynia with topical estradiol & testosterone
Rx: Estrogen & Testosterone

Introital Estradiol + Testosterone cream  n=50

Highest Vestibular Pain Score (max 10)

Burrows LJ, Goldstein AT. Sex Med. 2013; 1: 30–33
The treatment of vestibulodynia with topical estradiol & testosterone
Rx: Estrogen

Vaginal Estradiol pessary 25mcg x 6-10w n=29

Mixed contraceptive methods

Most switched to Norgestimate - EE35 “Cilest”

Given lidocaine gel 2%

Basic psychosexual advice (‘PLISS’)

No other intervention

Median Vestibular Pain Score (max 20) L=10, R=10

Greenhouse P. IUSTI Riga 2011

Intravaginal estrogen improves pain scores in provoked vestibulodynia
Vaginal Estradiol pessary 25mcg x 6-10w n=29

- Median Vestibular Pain Score (max 20)
  - L=10, R=10

Rx: Estrogen

Greenhouse P. IUSTI Riga 2011

Intravaginal estrogen improves pain scores in provoked vestibulodinia

Willcoxson signed rank test

\[ p < 0.001 \]

\[ \text{IQR 17-20} \]

\[ \text{IQR 0.5-8.0} \]
Rx: Estrogen + change Pill

Switch to least Androgenic COC   n=29

Before               After
COC Levonorgestrel-EE30   =12
Depo-Provera            =1
POP Desogestrel-only pill=3
Etonogestrel implant     =3
COC Gestodene-EE20       =2
**COC Norgestimate-EE35** =5
Condoms / Vasectomy      =3

Greenhouse P. IUSTI Riga 2011
Intravaginal estrogen improves pain scores in provoked vestibulodnia
**Rx: Estrogen + change Pill**

**Switch to least Androgenic COC**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>COC Levonorgestrel-EE30</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Depo-Provera</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>POP Desogestrel-only pill</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Etonogestrel implant</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>COC Gestodene-EE20</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>COC Norgestimate-EE35</strong></td>
<td>5</td>
<td>21</td>
</tr>
<tr>
<td>Condoms / Vasectomy</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

n=29

Greenhouse P. IUSTI Riga 2011

Intravaginal estrogen improves pain scores in provoked vestibulodnia
LPV Pain Score – CHANGES after Vaginal Estradiol

Number of cases: 29

P < 0.001

<table>
<thead>
<tr>
<th>Pain Score</th>
<th>Before</th>
<th>Nil</th>
<th>Partial</th>
<th>Good</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14-20</td>
<td>13-18</td>
<td>5-10</td>
<td>0-4</td>
</tr>
<tr>
<td>Percent</td>
<td>17%</td>
<td>31%</td>
<td>52%</td>
<td></td>
</tr>
</tbody>
</table>

Pain Score: 14-20 (17% improvement), 13-18 (31% improvement), 5-10 (52% improvement).
What else do we need?
Most women better with Estrogen AND - Estrogen does no harm...
No Control ??Bias/Placebo – needs RCT
Why do some women fail to improve?
Contraception choice is important
Other immunological factors?
In-depth psychosexual care
Other treatments?

Alternative to surgery?
Vestibulodynia Pathway

• Exclude unprovoked Vulvodynia
• Exclude Lichen sclerosis / dermatoses
• Exclude Candidiasis / Trichomoniasis
• Use topical Lidocaine / give ‘PLISS’

• Change contraceptive hormones
• Give local estrogen
• AVOID SURGERY

PRIMUM NON NOCERE
“And now we look for joys to come…”

Thank You

Thomas Rowlandson 1756-1827
Premier English Cartoonist